FUNCTIONAL EVALUATION IN PULMONARY TUBERCULOSIS SEQUELAE PATIENTS IN A TERTIARY CARE CENTRE – CHENGALPATTU

Dissertation submitted to

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

in partial fulfillment of the

regulations for the award of the degree of

M.D. (PHYSIOLOGY)

BRANCH - V

CHENGALPATTU MEDICAL COLLEGE & HOSPITAL

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

CHENGALPATTU , INDIA.

CERTIFICATE

This is to certify that this dissertation entitled **"FUNCTIONAL EVALUATION IN PULMONARY TUBERCULOSIS SEQUELAE PATIENTS IN A TERTIARY CARE CENTRE – CHENGALPATTU"** by the candidate **Dr.K.Parveen Bobby** for M.D (Physiology) Branch – V is a bonafide record of the research work done by her, under the guidance of **Dr.C.Hemachandrika M.D.** Associate Professor, Formerly Head of the Department of Physiology, Chengalpattu Medical College, during the period of study (2013 - 2016), in the Department of Physiology, Chengalpattu Medical College, Chengalpattu . I also certify that this dissertation is the result of the independent work on the part of the candidate

Signature of the Guide	Associate Professor and Head of Department
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The Dean

Chengalpattu Medical College

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DECLARATION

I hereby declare that this dissertation entitled "Functional Evaluation In Pulmonary Tuberculosis Sequelae Patients In a Tertiary Care Centre – Chengalpattu" is a bonafide and genuine research work done by me under the guidance of our Professor Dr.C.Hemachandrika M.D., Associate Professor and Formerly Head of Department, Department of Physiology, Chengalpattu Medical College, Chengalpattu.

This dissertation is submitted to the Tamilnadu Dr. M.G.R Medical University, Chennai in partial fulfillment of the university requirements for the award of degree M.D in physiology.

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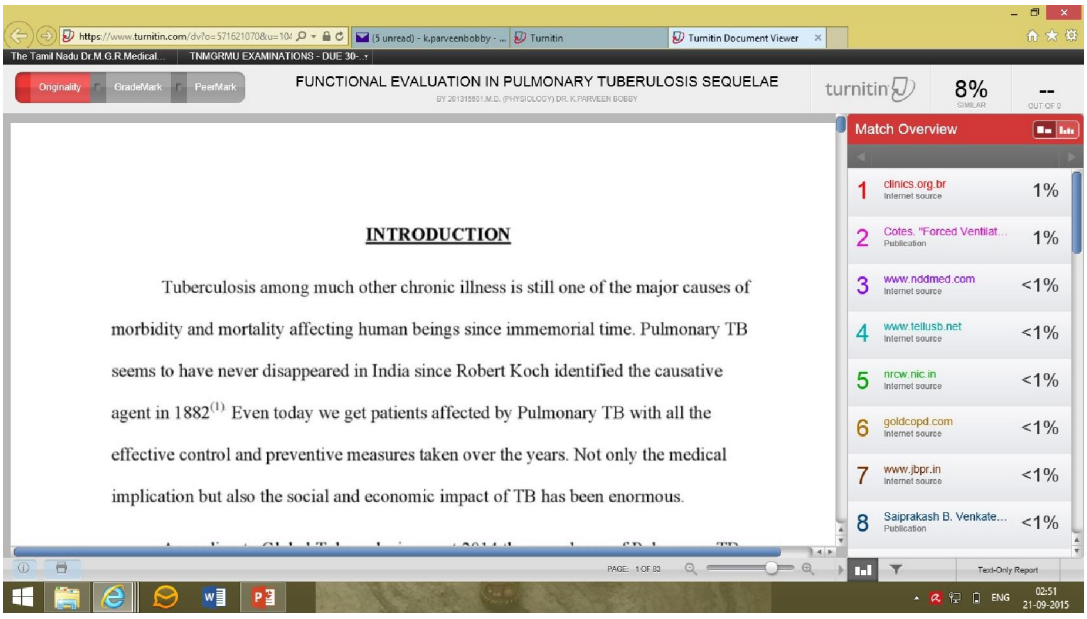
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INTRODUCTION
Tuberculosis among much other chronic illness is still one of the major causes of morbidity and mortality affecting human beings since immemorial time. Pulmonary TB seems to have never disappeared in India since Robert Koch identified the causative agent in 1882(1) Even today we get patients affected by Pulmonary TB with all the effective control and preventive measures taken over the years. Not only the medical implication but also the social and economic impact of TB has been enormous.
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APPROVAL OF ETHICAL COMMITTEE

To

Dr.K.Parveen Bobby,
MD Physiology
(2nd Year),
Chengalpattu Medical College,
Chengalpattu.

Dear Dr.

The Institutional Ethical Committee of Chengalpattu Medical College reviewed and discussed your application to conduct the clinical / dissertation work entitled

"FUNCTIONAL EVALUATION IN PULMONARY TUBERCULOSIS SEQUELAE PATIENTS IN A TERTIARY CARE CENTRE-CHENGALPATTU".

ON 11.06.2014

The following documents reviewed

1. Trial protocol, dated _____version no
2. Patient information sheet and informed consent form in English and / or
   vernacular language.
3. Investigators Brochure, dated _____version
4. Principal Investigators current CV
5. Investigators undertaking

The following members of the Ethics committee were present at the meeting held on

Date 11.06.2014 Time 11.30 Noon Place Chengalpattu Medical College

Approved _____ Chairman Ethics Committee

11/6/14 Member secretary of Ethics Committee.

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8. Layperson : Mr.Dilli

We approve the clinical trial to be conducted in its presented form

The Institutional Ethics Committee expects to be informed about the progress of the study and any SAE occurring in the course of the study, any changes in protocol and patient information / informed consent and asks to provide copy of final report.

Yours sincerely

11/6/14

Member secretary, Ethics Committee

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LIST OF ABBREVIATIONS

ABG	Arterial Blood Gas
ANOVA	Analysis Of Variance
BMI	Body Mass Index
BTPS	Body Temperature Pressure and Saturated with water vapour
DLCO	Diffusion Capacity of Lungs
FEF 25-75%	Forced Expiratory Flow
FET	Forced Expiratory Time
FEV1	Forced Expiratory Volume in 1st Second
FRC	Functional Residual Capacity
FVC	Forced Vital Capacity
FVL	Flow Volume Loop
HIV	Human Immunodeficiency Virus
MEFV	Maximal Expiratory Flow Volume
MMFR	Maximal Mid expiratory Flow Rate
MVV	Maximum Voluntary Ventilation
PEFR	Peak Expiratory Flow Rate
PFT	Pulmonary Function Test
PT	Pulmonary Tuberculosis
S.D	Standard Deviation
TB	Tuberculosis
TIMPS	Tissue Inhibition Of Matrix Metallo Proteinases
TLC	Total Lung Capacity
VC	Vital Capacity
V_T	Tidal Volume

Recording with Easy on PC Spirometry.

ABSTRACT

Title:

Functional Evaluation In Pulmonary Tuberculosis Sequelae Patients In a Tertiary Care Centre – Chengalpattu

Background:

Pulmonary Tuberculosis can cause chronic impairment of lung function even after completion of anti-TB treatment. Several factors predict the deterioration of pulmonary function in treated cases. The time course for change in pulmonary function and risk factors have not been well studied so far.

Aim & objective:

The present study aimed to investigate the trends in changes in pulmonary function and factors associated with the sequelae changes in lung in patients who were treated for pulmonary Tuberculosis.

Materials & method:

120 subjects both male and female of age 30-60 years who had completed anti-TB treatment 18 months back and within 5 years of completion of treatment were included in the study. Pulmonary function analysis was done by Spirometry. FVC, FEV_1, FEV_1/FVC were taken for analysis.

Results:

The pattern of lung function impairment observed in the study were restrictive and mixed pattern in majority of subjects, only 13 out of 120 subjects had normal pattern in spirometry. The impairment of lung function was found to increase incrementally with increase in lag time, number of episodes of treatment and duration after completion of treatment.

Conclusion:

As we have limited resources for the management of restrictive and mixed pattern of impairment it is essential that for patients with significant respiratory symptoms and multiple risk factors, periodical assessment of pulmonary function should be done to monitor the progress of lung function. This also helps in early intervention like pulmonary rehabilitation to improve the quality of life in treated pulmonary Tuberculosis patients.

Keywords:

Pulmonary Tuberculosis sequelae, Spirometry, Restrictive pattern and Mixed pattern of Lung function impairment.

INTRODUCTION

Tuberculosis among much other chronic illness is still one of the major causes of morbidity and mortality affecting human beings since immemorial time. Pulmonary TB seems to have never disappeared in India since Robert Koch identified the causative agent in 1882.[1] Even today we get patients affected by Pulmonary TB with all the effective control and preventive measures taken over the years. Not only the medical implication but also the social and economic impact of TB has been enormous.

According to Global Tuberculosis report 2014 the prevalence of Pulmonary TB worldwide is around 9 million and in India the incidence is 2.2 million and prevalence is 2.8 million cases. [2]

There are many studies which focused on the pathophysiology, diagnosis, and treatment of Pulmonary TB but only a few studies were done so far on the after effects of PT infection in lungs.

In the few studies that are being done on evaluation of Lung functions in PT Sequelae patients there are concrete evidences stating that there is permanent functional deterioration in these patients.

Many studies say that the obstructive pattern of lung damage is the commonest finding. But recent studies say that there are more number of patients with restrictive and mixed pattern of damage. [3,5]

According to previous studies the changes are more pronounced during 13-18 months after completion of anti-TB treatment [3,4] In our area where people seek medical help at a very late stage, there is involvement of both bronchi & parenchyma leading to extensive damage of both. It is important to identify patients with deterioration of pulmonary function after the completion of treatment because it affects the quality of life of the patients to a great extent.

This evaluation can be done by an easy and accessible technique called SPIROMETRY.

TUBERCULOSIS

The word Tuberculosis was derived from the Latin word "TUBERCULA" meaning small lump. [6]

HISTORY

TB appears to be as old as humanity itself. Skeletal remains of human being affected by TB which was dating back to 8000 BC was found in Germany. Ancient Hindu and Chinese writings documented the presence of disease. Best proof of TB in ancient world has come from mummy of an 8yr old boy who lived 700 AD showed evidence of Pott's disease in X-rays and smear. [7]

CAUSATIVE AGENT

It was Robert Koch who was the one to demystify the cause of TB by identifying the bacilli in 1882. [1]

Pulmonary TB is commonly caused by Mycobacterium Tuberculosis which are Gram positive bacteria of about 0.2 to 0.6 micro meter by 1.0 to 10 micrometre in size. They survive best under temperature of 30ºc to 39ºc. They are obligate pathogens and they cannot multiply outside human or animal body.

The bacilli can remain viable for many years in tissues of even healthy people. It runs a chronic and protracted course when they produce a disease. [6]

TRANSMISSION

TB bacilli can affect almost all the organs in the human body, but lungs is the commonest portal of entry in many cases.

Pulmonary TB is clearly an air borne disease and is caused by inhalation or droplet nuclei with 1 to 3 TB bacilli in it. These droplets are released into the atmosphere by an infected person through coughing, sneezing, even while speaking.

The patients who has productive cough and whose sputum is smear positive for bacilli, they discharge numerous droplet nuclei with numerous bacilli in it. The common risk factor for transmission is poor health, poor socioeconomic status, poor sanitation and crowded living conditions. [7]

PATHOGENESIS

After entry into the lungs the TB bacilli evoke immunity within 2 to 8 weeks of infection in a normal healthy individual.

The alveolar macrophages get activated and release interleukins which in turn stimulate T cells to release interferon gamma. These activated T lymphocytes forms a granuloma within which the bacilli are sequestered as dormant foci.

In 90% people provided they have adequate cell mediated immunity, these bacilli remain as dormant foci, i.e. these people are infected but not diseased. This is called primary infection or primary tuberculosis.

If any defect in immunity arises some people may have an early progressive disease within 5 years of exposure. Others may experience recrudescent disease even after several decades. This is called reactivation or post primary tuberculosis.

This reactivation of the dormant bacilli may occur commonly in conditions like diabetes mellitus, HIV, chronic renal failure, vitamin D deficiency. [7,8,9]

STAGES OF PATHOPHYSIOLOGY

STAGE I :

TB bacilli are engulfed by alveolar macrophages. There is no growth of bacilli inside the macrophages.

STAGE II: (symbiotic stage)

It occurs 7 to 21 days after infection. There is growth and multiplication of bacilli within the macrophages in a logarithmic scale without damage to the host.

STAGE III (caeseous necrosis stage):

It is a delayed type of hypersensitivity. The activated T cells kills the bacilli laden macrophages forming a caseation. The bacilli can still survive but cannot multiply inside the caeseous material due to anoxia, acidic pH.

STAGE IV:

Cell mediated immunity of the host plays a major role in this stage. If the immunity is good, the bacilli are destroyed. If the immunity is poor, then the bacilli escapes from the caseation and enters lymph nodes and from there through the lymphatic circulation it enters blood circulation.

STAGE V:

Liquefaction of caeseous centre occurs and bacilli for the first time multiply extra cellularly outside the macrophages and through haematogenous spread it is taken to various other organs.

At the same time tuberculin like products are released by bacilli causing necrosis and erosion of bronchial walls and a cavity is formed. Now the bacilli enter into the bronchial tree and spreads to the other parts of the lung and also to outside environment infecting other people. [11,12,13]

CLINICAL PRESENTATION

Patient often shows a composite picture in 4 to 6 weeks after infection, i.e, during primary TB, most of the patients are asymptomatic or may experience minimal symptoms like fever and malaise. Ordinarily until disease is far advanced

the symptoms are minimal and the frequency of symptoms also differs whether the patient has primary or reactivation TB.

During reactivation stage productive cough with sputum and hemoptysis occurs especially during liquefaction stage. [7]

TB IN OLD AGE

The picture differs in old age compared to young adults. They present more commonly with dyspnoea and significant co morbidities. The typical symptoms like fever and hemoptysis are less likely to manifest in old age. [13]

PULMONARY TB & PATTTERN OF DAMAGE IN LUNGS

PATHOGENESIS OF OBSTRUCTIVE AIRWAY DIEASE

The bronchial tree is affected by any one of the following mechanisms

a) Most commonly the tracheo-bronchial lymph nodes compress the brochi. If this obstruction is complete the lung parenchyma distant to it may be atelectatic. If this obstruction is incomplete, it acts like a ball-valve causing obstructive emphysema.

b) Implantation of organism from infected sputum causes inflammatory changes in trachea-bronchial tree. If the patient has good immunity this results in increased mucus production causing obstruction or the inflammatory cells may release cytokines which cause destruction of bronchial wall causing bronchiectasis.

c) Erosion of lymph nodes into trachea bronchial tree can cause bronchiectasis.

d) Direct spread from adjacent parenchyma or spread by haematogenous route may occur.

All these mechanisms lead to stenosis of bronchial tree despite of treatment there by leading to collapse of dependent parts of lung. [14,15]

PATHOGENESIS OF RESTRICTIVE LUNG DISEASE

In majority of patients the initial focus subsides with cicatrisation, scar formation and calcification even when their natural immunity evades the disease. If the person is exposed to repeated episodes of extensive PT the infected parenchyma heals with fibrosis causing loss of lung tissue.

Recently the role of matrix metalloproteinases in destruction of lung tissue is being proposed by many studies. Lung extra cellular matrix is formed by fibrillary collagen which is highly resistant to enzymatic cleavage except only matrix metalloproteinases which can digest all the components of extra cellular matrix.[7,14,15]

P.T.Elkington et al has proved in their studies that in TB affected lungs the alveolar macrophages express matrix metalloproteinases – 1 & 9. There is also evidence of decrease in tissue inhibition of matrix metalloproteinases (TIMPS). These two factors result in digestion of extra cellular matrix substances thereby causing destruction of lung tissue. [28,30]

CHANGES IN SMALL AIRWAYS

The patency of small airways is maintained by surrounding parenchyma which provides a radial traction of bronchioles.

When the extracellular matrix in the surrounding parenchyma is destroyed by fibrosis the radial traction is lost and there may be distortion and narrowing of small airways. [16]

RESPIRATORY SYSTEM

The structure of respiratory system is unique to suit its primary function of transport of gases in and out of the body.

ANATOMY

Airflow through respiratory system is by 3 interconnecting structures – upper airways, conducting airways and alveolar airway (also called as lung parenchyma).

UPPER AIRWAY

It includes nose, mouth, pharynx and larynx.

CONDUCTING AIRWAYS

It starts from trachea and branches out 23 times till it reaches alveolar sacs. The first 16 generation form the conducting zone and it includes large and small bronchi, small bronchioles and terminal bronchioles.

This structure consists of a lining mucosa, secretory cells, smooth muscles in their walls and an enveloping connective tissue interspersed with cartilage. Towards

terminal bronchioles there is decrease in cartilage and absence of secretory cells, but the smooth muscles in their walls are prominent.

ALVEOLAR AIRWAY (LUNG PARENCHYMA)

This includes last 7 generations and made up of transitional respiratory bronchioles, alveolar duct and alveoli.

There are around 300 million alveoli in human lungs. The surfactants released by alveolar cells decreases the surface tension. Interstitium is a microscopic anatomical space bound by basement membrane of epithelial cell of alveoli and endothelial cell of pulmonary capillaries. It consists of collagen and reticulin fibers which create a helical network of connective tissue around the alveoli and respiratory airway walls.

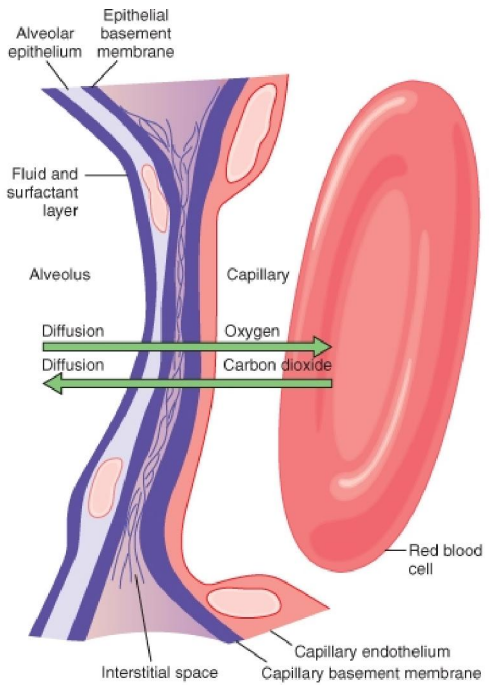
The lungs are conglomerate of alveoli bounded by chest wall and diaphragm and lie within pleural cavity. The average volume of lung is 3.5 litres and they weigh 900gms approximately.

Both the lungs and chest wall are elastic in nature and they can expand and recoil. This elasticity is conferred by elastic tissue in airway and alveolar wall, and also by connective tissue in the inter alveolar space and by surfactant. [16,18,19]

RESPIRATORY UNIT

It is composed of respiratory bronchiole, alveolar ducts and alveoli. The alveolar wall has network of interconnecting capillaries. So that exchange of gases occurs between alveoli and capillaries. [20]

Figure 1: Respiratory membrane



This is the structure through which exchange of gases takes place.

The layers of the structure are

1) Fluid layer containing surfactant

2) Layer of alveolar epithelium

3) Epithelial basement membrane

4) Thin interstitial space between alveoli and capillaries

5) Capillary basement membrane

6) Endothelial cell layer of capillaries [20]

INSPIRATION AND EXPIRATION

Inspiration is an active process. The muscles involved are diaphragm, external intercostal muscles, sternocleidomastoid muscle, serratus anterior muscle, scalene muscle. When these muscles contract they increase the lung volume.

The intra pleural pressure becomes more negative from -2.5mm Hg to -6mmHg during inspiration. This is created by expansion of chest wall which pulls the lung along with it with such great force.

Expiration during quiet breathing is passive. At the end of inspiration, the inspiratory muscles relax and also due to elastic recoiling of lung the chest wall is pulled back to its original position. Now the intra pleural pressure becomes slightly positive and air flow out of the lungs.

At the end of expiratory process, the recoiling force of lungs and the recoiling force of the thoracic cage balance each other and now the intra pleural pressure becomes -2.5 mm Hg. [17]

PULMONARY DEFENSE MECHANISM

At all levels of respiratory tract specific and nonspecific defense mechanisms exists to protect the respiratory system.

Epithelial cells of conducting airway secrete IgA, surfactant protein A and B, various proteases, peptidases that kills the microbes directly. They also secrete chemokines and cytokines that attract immune cells there by killing the microbes indirectly.

The dichotomous branching of airway traps the smaller particles and clears it by coughing and mucociliary escalation.

The alveoli have pulmonary alveolar macrophages which secrete cytokines to attract the granulocyte and initiate immunological reaction. But this action is a two edged sword for the pulmonary alveolar macrophages may also release lysosomal products in extracellular space to cause inflammation of the Interstitium that heals with fibrosis. [13,17]

PATHOGENESIS OF OBSTRUCTIVE LUNG DISEASE

Inflammation of airways or bronchial hyper reactivity may lead to increased mucus production, decreased ciliary action and loss of elasticity of bronchial wall. These lead to obstruction of airways. [19]

PATHOGENESIS OF RESTRICTIVE LUNG DISEASE

Normally interstitial space has minimal connective tissue, extracellular matrix and minimal inflammatory cells in them. This allows efficient gas exchange between alveoli and capillaries. If any inflammation of interstitium occurs, the lungs responds to the damage and try to repair the damage. If the inflammation persists or if there is imperfect repairing process occurs, then this may lead to permanent damage of lung parenchyma resulting in restrictive lung disease. [19]

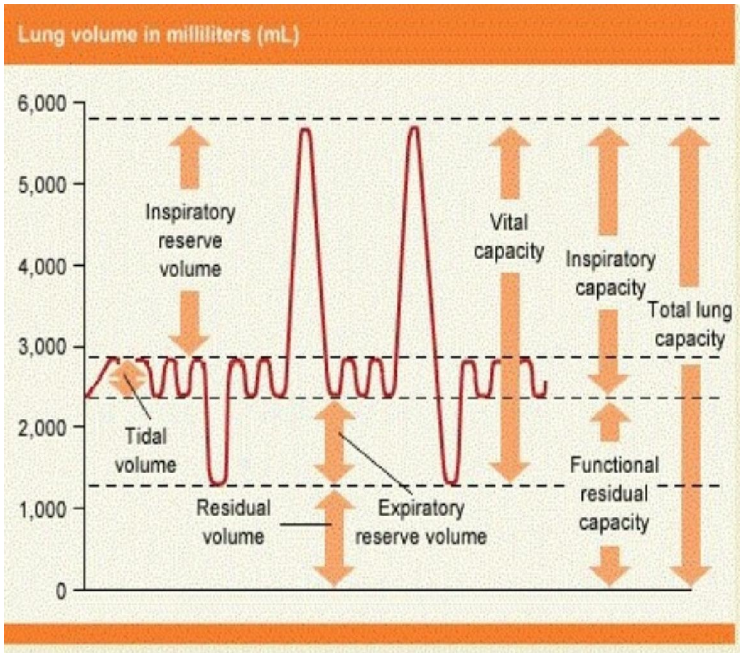
LUNG VOLUMES AND CAPACITIES

Lung volume determinants usually include the vital capacity and its subdivision along with functional residual capacity. From these two basic measurements the remaining lung volumes and capacities can be calculated.

There are four lung volumes. They are

1. **Tidal volume** is the volume of air inspired or expired during quiet breathing and is about 500ml.
2. The amount of air inspired with maximum inspiratory effort above the normal tidal volume is called **inspiratory reserve volume**: It is about 3000ml.
3. The **expiratory reserve volume** is the volume of air expired with maximum expiratory effort after the normal tidal expiration: This normally amounts to about 1100ml.
4. The volume of air remaining in the lungs after the forceful expiration is known as **residual volume**: It is normally about 1200ml.

Figure 2: Lung volumes and capacities



The pulmonary capacities are

1. The maximum amount of air inspired after completing the tidal expiration is defined as **inspiratory capacity** and is about 3500ml.

2. The **functional residual capacity** is the amount of air remaining in the lung at the end of normal expiration and is about 2300ml.

3. The **vital capacity** is the maximum amount of air expired forcefully after a maximum inspiratory effort and is about 4600ml.

4. The **total lung capacity** is the volume of air present in the lung after a maximum inspiration and is about 6 litres. [20]

INDICES BASED ON VOLUME

1) FORCED VITAL CAPACITY (FVC)

It is defined as the maximum volume of air expired forcefully and rapidly after a maximal inspiration.

Normally FVC equals VC or FVC and VC should be within 200ml of each other. When FVC is < 80% of predicted value it is abnormal. But low FVC is a nonspecific finding.

FVC may be low in both obstructive and restrictive disorder. But in restrictive disorder FVC is too low compared to FEV_1.

2) FEV_1

It is the volume of air expired in first second of an FVC manoeuvre. When it is < 80% of predicted value it is considered to be abnormal. It is also a non specific measurement.

FEV_1 may be low in both obstructive and restrictive disorders, but in obstructive disorder FEV1 is considerably low when compared to FVC.

3) FEV_1 / FVC ratio (or) FEV_1%

The FEV1 expressed as a percentage of VC or FVC. Normal value is 70%

$FEV1\% = (FEV1/FVC) \times 100$

The relationship is a component of most lung function reports.

4) FEF $_{25-75\%}$

Forced expiratory flow over the middle half of the FVC manoeuvre. It is an indicator of status of medium to small airways. Normal value for healthy young adults is around 4 to 5 litres per second. When it is measured in percentage the normal value is 65% of predicted value.

5) MAXIMUM VOLUNTARY VENTILATION (MVV)

It is the maximum volume of air expired in a specific period of time (12 sec for normal subjects). It tests the overall function of the respiratory system. It is influenced by airway resistance, respiratory muscle, compliance of the lung and chest wall and ventilatory control mechanisms. Values in healthy young men average between 150 – 200 L/min. MVV is decreased in patients with moderate or severe obstructive disease. MVV may be normal in patients who have restrictive pulmonary disease. They can compensate by performing the MVV manoeuvre with VT and breathing rates.

6) SLOW VITAL CAPACITY

The volume of gas measured from a slow, complete expiration after a maximal inspiration, without forced or rapid effort is known as vital capacity. It is also referred to as the slow vital capacity, distinguishing it from forced vital capacity.

7) **PEAK EXPIRATORY FLOW (PEF)**

The maximal expiratory flow achieved during a maximum forced expiration initiated at TLC. PEF primarily measures large airway function. Effort dependence of PEF makes it a good indicator of patient effort during spirometry. It is particularly useful for monitoring asthma patients at home. [18,21,22]

INDICES BASED ON TIME

FORCED EXPIRATORY TIME (FET)

The time taken to expire a specified portion of the forced vital capacity is known as forced expiratory time (FET). If it is > 4 second it indicates some degree of airflow obstruction. [22]

PULMONARY FUNCTION TESTS

Pulmonary function tests are age old and very important tests to assess the function of respiratory system in a person. They provide knowledge about the clinical condition, diagnosis and prognosis of a disease.

Normally a person attains maximal lung function around 20 to 25 years of his / her age. After 30 to 35 years of his / her age there is decline in lung function.

The lung function decline to a moderate extent even before clinical symptoms and signs develop. So the assessment of severity of disease is difficult with symptoms and signs alone, which may lead to inadequate treatment and control of disease. So early measurement of lung function test is very important for

early intervention and control, and also to monitor the progress of the disease.[19,21,23]

The important factors that determine the ability of lungs to exchange gases effectively are as follows.

Factors contributing for ventilation:

1) The diaphragm and other thoracic muscles which are essential for expanding the lungs and thoracic cavity to create a sub atmospheric pressure.
2) The patent airways which allows the gas to reach the alveoli.

Factors determining the diffusion and perfusion of lungs:

1) The intact and effective respiratory membrane for the diffusion of oxygen and carbon dioxide across them.
2) The normal functioning of cardiovascular system to provide adequate blood supply to the lungs.

The pulmonary function tests provide valuable information about all the above processes of ventilation, diffusion and perfusion.[14]

Based on the aspects of lung function they measure, the pulmonary function tests are categorized as:

1) **Airway function test** – VC, FVC, FEV_1, PEFR, FEF
2) **Lung Volume and Ventilation Test** – FRC, TLC, Minute ventilation

3) **Diffusion Capacity Test** – D_{LCO}

4) **Blood Gas and Gas Exchange Test** – ABG, pulse oximetry, capnography

5) **Cardiopulmonary Exercise Test** – Test with exhaled gas analysis, Test with blood gas analysis

6) **Metabolic Measurement** – resting energy expenditure, substrate utilisation

Among these the airway function and lung volume are almost always measured with spirometry [21]

SPIROMETRY

Spirometry is a basic, easiest but powerful tool that can detect and differentiate the lung disorders and is also used as a tool for follow up of patients with pulmonary disorders. It is very useful in determining the pattern of lung dysfunction.

However, spirometry must be performed correctly because it may yield a false positive response if performed poorly.

HISTORY OF SPIROMETRY

In 1800 John Hutchinson developed a simple water seal spirometer with which he measured a parameter what he called as vital capacity / vital breath. He observed that vital capacity was related to standing height of the patient. He also developed a table to estimate expected vital capacity for a healthy person.

Borelli in 1679 measured the volume of air inhaled by a single deep breath.

In 1788 the need for temperature correlation was pointed out by Goodwyn.

In 1800 Davy measured the residual volume by gas dilution method.

In 1831 Thackrah showed that the volume of air is less in women than men.

In 1956 Dubois and colleagues developed a method called whole body plethysmograph.

In 1930s Barach observed that the patients with asthma exhaled more slowly than healthy individuals. He was the one who noted that airflow out of the lungs was important in determining obstructive airway disease. Subsequently he used kymograph to display VC changes as a Spirogram.

In 1950 Gaensler used a micro switch in conjunction with water sealed spirometer to time FVC. He observed that healthy individual exhaled approximately 80% of their FVC in 1 second and almost all of FVC in 3 second. He used the FEV_1 to assess airway obstruction.

In 1955 Leuallen and Fowler demonstrated a graphical method to assess air flow. They measured airflow between 25% and 75% points on a forced expiratory spirogram. This was described as maximal mid expiratory flow rate (MMFR) or forced expiratory flow 25-75% ($FEF_{25-75\%}$).

In the late 1950s Hyatt and others used the flow volume display to assess airway function. The tracing was called maximal expiratory flow volume curve

(MEFV curve). By combining this with inspiratory manoeuvre a closed loop called flow volume loop (FVL) was displayed.

In 1960s Wright used peak flow to monitor asthmatics. PEF is measured using a flow sensing spirometer / peak flow meter.

Maximum voluntary ventilation (MVV) was described in 1941. Cournand and Richards called it originally the maximal breathing capacity. MVV gives an estimation of the peak ventilation available to meet physiological demands.

Nowadays modern computerized pulmonary function systems allow very sophisticated data handling and storage, graphic display of manoeuvres, accurate calculation and enhanced reporting method. They include physical transducers, analog to digital converters and computer software to process and record the data. Microprocessor based portable spirometers are now available. [21]

TYPES OF SPIROMETERS

Based on the principle by which they work the spirometers are of two types.

I) Volume displacement spirometers

The amount of air exhaled or inhaled within a certain time is recorded by these types of spirometers. The following are widely used volume displacement spirometers.

1) Water seal spirometer
2) Dry rolling seal spirometer
3) Bellows spirometer

II) Flow sensing spirometers (pneumotachometer)

They measure how fast the airflows in or out as the volume of air inhaled or exhaled increases. The common types are:

1) Rotating vanes (turbine)
2) Pressure differential flow sensing spirometer
3) Hot wire anemometers
4) Pitot tube flow sensing spirometers
5) Ultrasound devices. [21]

STANDARDIZATION OF SPIROMETRY

According to American Thoracic Society the spirometers are standardized as follows:

It should record at least FVC and FEV1.

It should record a flow volume curve or a flow volume loop or both.

It should be able to measure up to 15 seconds for FVC.

It should have a capacity of 8 litres.

It should measure volume within < 3% error or within 0.05 litres of a reference value whichever is greater.

It should measure flow within <5% error or 0.2 litres per second whichever is greater.

The values given by spirometer are corrected for body temperature, ambient pressure and saturated with water vapour (BTPS).

It can be calibrated with a 3 litres syringe. [24]

INDICATIONS FOR SPIROMETRY

1) To detect presence or absence of lung dysfunction
2) To assess severity of lung disease
3) To monitor the disease progression
4) To assess the efficacy of treatment given
5) To measure the effects of occupational and environmental exposure of air pollutants
6) To assess fitness of patient prior to surgical procedures.
7) To quantify the impairment or disability. [19,25]

CONTRAINDICATIONS FOR SPIROMETRY

1) Any respiratory infections
2) Recent myocardial infarction within 1 month prior to the procedure.
3) Unstable cardiovascular status.
4) Haemoptysis of any cause.
5) Pneumothorax
6) Recent surgeries of eye / thorax / abdomen

7) Stress incontinence.

8) Dementia or confused patient.

9) Oral or facial pain exaggerated by the mouth piece. [19,25]

RECORDING OF SPIROMETRY

It is recorded both graphically and numerically. Graphically it is recorded as

1) Spirogram – volume versus time graph

2) Flow rate versus volume – it can be either

   a) Flow volume curve when only expiratory flow is recorded

   b) Flow volume loop when both expiratory flow and inspiratory flow is recorded. [21,22]

Figure 3

Volume vs time graph (spirogram)

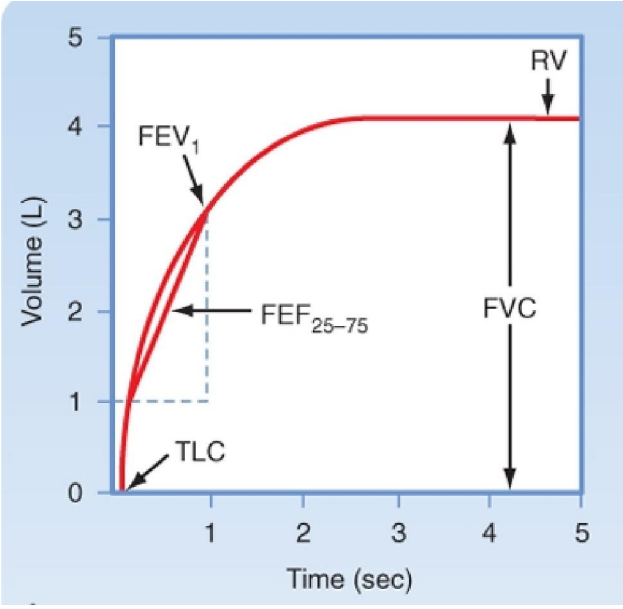
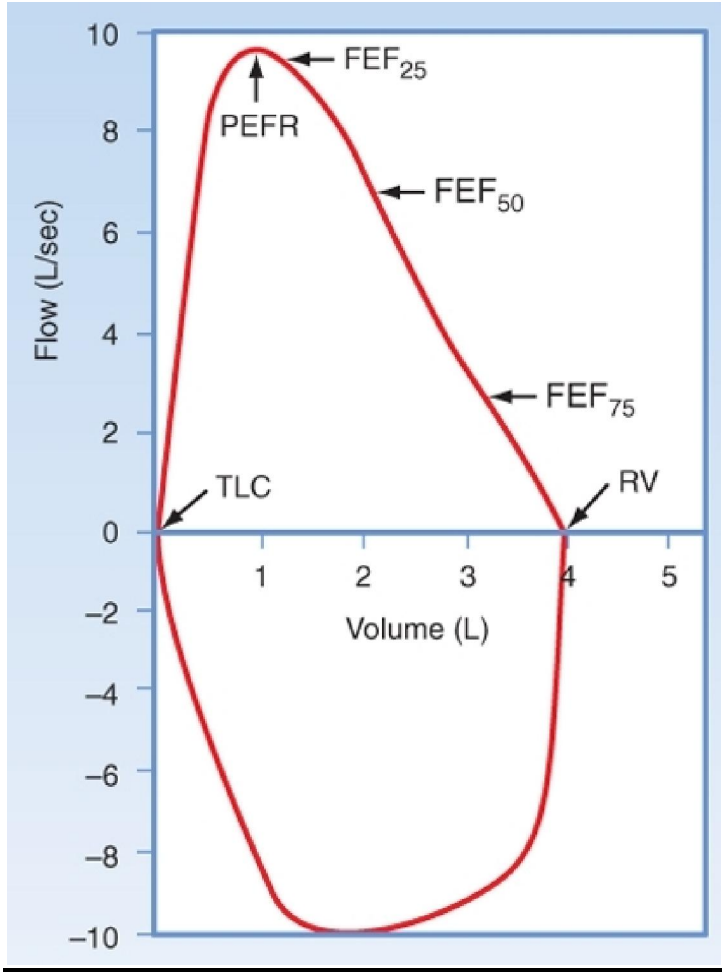


Figure 4: Flow – volume loop



Flow is plotted on the vertical axis and volume is plotted on the horizontal axis.

Expiratory flow is plotted upward and inspiratory flow is plotted downward.

Peak flows for expiration and inspiration (PEF and PIF) can be read directly and the instantaneous flow (FEF) at any point in the FVC also can be measured directly.

LUNG DISORDERS AND ITS PATTERN IN SPIROMETRY RESULTS

Normal value – FEV_1 and FVC >80% predicted value

- FEV_1 / FVC ratio >70% of predicted value

Obstructive lung disorders

- FEV_1 <80% of predicted value
- FVC normal or reduced (if reduced usually to a lesser degree than FEV_1)
- FEV_1 / FVC ratio <70% of predicted value

Restrictive lung disorder

- FVC <80% of predicted value
- FEV_1 normal or reduced (if reduced usually to a lesser degree than FVC)
- FEV_1 / FVC ratio 70% or > 70% of predicted value

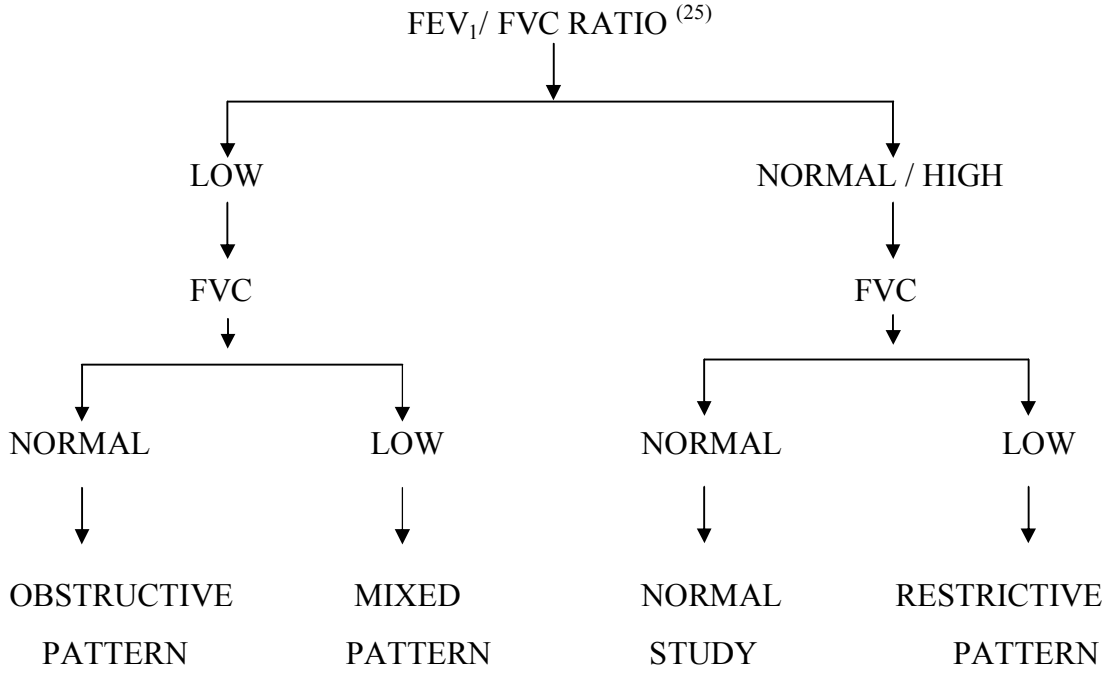
Mixed function disorder (both obstructive and restrictive)

- FVC and FEV_1 <80% of predicted value
- FEV_1 / FVC ratio <70% of predicted value [31]

Table I: Interpretation of Spirometry data

PFT PARAMETERS	OBSTRUCTIVE PATTERN	RESTRICTIVE PATTERN	MIXED PATTERN
FEV_1	Reduced	Reduced / Normal	Reduced
FVC	Reduced / Normal	Reduced	Reduced
FEV_1 / FVC	Reduced	Normal / Increased	Reduced

Figure 5: Interpretation of patterns of lung function impairment



REVIEW OF LITERATURE

REVIEW OF LITERATURE

Dye C et al in their studies have stated that despite predictions of global decline in incidence of pulmonary tuberculosis, still new cases nearing 10 million has been reported in 2010 worldwide. This study has reviewed the changing relationship between the host i.e. human body and the causative agent i.e. mycobacterium tuberculosis that could explain the persistence of TB. Whatever the technology used, successful control depends on the social, institutional & epidemiological context in which it is applied**.** [32]

The chronic impairment of lung function increases with increase in number of episodes of tuberculosis. The effect of TB on lung function can be prevented by early detection and control of other risk factors such as occupational exposure, socioeconomic factors etc. [33]

On investigating the trends in changes in pulmonary functions and the risk factors responsible for deterioration of pulmonary function, it was found that the nadir of pulmonary function occurred approximately 18 months after completion of treatment for TB. The risk factors included are smear positive disease, extensive lung involvement prior to treatment, prolonged treatment, and reduced radiological improvement after treatment. So it is important that pulmonary function tests are done as a routine follow up especially 18 months after the completion of anti-tuberculous treatment. [3]

Inflammatory tissue damage is the main pathogenesis for destruction of lung tissue, the tissue damage is caused by digestion of extracellular matrix substance by decreased tissue inhibition of matrix metalloproteinases. [28]

In progressive tuberculosis patients lung remodeling (i.e. healed cavitation, fibrosis,etc.) occurs by dysregulation of granulomatous turnover, liquefaction necrosis and pathological scarring. [27]

TB sequelae changes occur more commonly in young age and men: women ratio is 2:1. Systemic complication of pulmonary tuberculosis are not more common and main factor in development of sequelae changes is due to local lung tissue damage. [35]

Neeta singla et al in their study on screening for lung function impairment in patients with post treatment period of 22 ± 14.7 months had found that 96% of patients were found to have abnormal PFT. Out of this 66% had mixed pattern, 19% had pure restrictive pattern and 11% had pure obstructive pattern of damage. [36]

Nefedov et al in their study on functional evaluation of patients with chronic fibrocaseous tuberculosis found that lung function defect was found in 96.8% of patients under their study. Among these considerable and drastic changes in lung volume and capacities occurred in 90.2 patients and mild impairment of bronchial patency and pulmonary exchange function in 90.3. [37]

Clinico physiological examination of patients with destructive pulmonary tuberculosis showed that restriction pattern of damage and decline of elasticity of

lung tissue is the most common manifestation. The bronchial patency disorder and disorders in exchange of gas occurs less common. [38]

In a study in which spirometry was done in adult treated TB patients presenting with dyspnoea, all 3 types of lung function damage viz restrictive, obstructive, mixed pattern was found. [39]

There is high rate of morbidity among cured pulmonary tuberculosis patients even 14years after completion of treatment causing deterioration of their Quality of life. The predominant impairment are restrictive and mixed pattern disease. [40]

Pulmonary tuberculosis results in partial reduction of ventilation and perfusion. Normal lung function was seen in non cavitary disease. Mild restriction is seen in cavitary disease. [41]

In elderly patients isolated mid or lower lobe involvement is common. Consolidation and large opacity mimicking mass is seen in elderly patients. [42]

All cases of cured pulmonary tuberculosis even though patients are asymptomatic, they are prone to have pulmonary function impairment. There is a relationship between positive radiological score and severity of defect in lung function i.e. greater radiological sequelae implies severe pulmonary impairment. [43]

Even after completion of successful treatment in non-obstructive cases of lung impairment change in vital capacity was found to be 27.7ml/year. Decrease in FEV was found in 28.8ml/ year. [44]

The accuracy of spirometric measures of FVC and expiratory flow rates in diagnosing presence of restrictive impairment was studied by Shaw et al. according to this study <60% of patients with a classical restrictive pattern in Spirometry had pulmonary restriction confirmed by measurement of lung volumes. [45]

Interpretation of restrictive pattern identified by means of spirometry can be made accurately by incorporating the magnitude of reduction in FVC and percentage difference between FEV_1 and FVC. [46]

Venkateshiah et al in their study aimed at determining the utility of spirometric measurements of FVC, FEV_1 and FEV_1/FVC ratio in diagnosing restrictive pattern. They have concluded that FVC < Lower limit of normal and FEV_1/ FVC within normal range has a positive predictive value of up to 73.9% in diagnosing restrictive pattern. They have also concluded that FVC can be used as a criteria to exclude restriction with higher reliability. [47]

Eric Walter Petura Yone et al had done a study to assess the clinical impact of low FEF 25-75% in treated Pulmonary Tuberculosis patients. They had fixed a cut off value of 65% for FEF25-75% below which patient was diagnosed to have distal airway obstruction. In their study they had a correlation of time lag of >12 weeks and occurrence of FEF25-75% <65% in these patients. [48]

Evaluation of physical functional capacity in pulmonary tuberculosis sequelae patients of age 50-65 years when compared with age matched healthy individuals showed a significant decrease in functional capacity in pulmonary tuberculosis sequelae patients due to exercise induced hypoxia. [49]

A study on Quality of life using SF-36 questionnaire which was conducted in a Tuberculosis unit in south India with 436 patients who had completed treatment 1 year prior to the study has shown that the decrease in Quality of life after the disease was associated with age, literacy, income, smoking, alcoholism, persistence of symptoms. [50]

Reduction in functional exercise capacity due to increase in work of breathing in chronic respiratory illness makes the patients to be depressed and socially isolated. The functional disability and repeated hospitalization decreased their efficiency in work and pose a socioeconomic burden. So Pulmonary rehabilitation as a multidisciplinary and comprehensive non pharmacological intervention has emerged as a recommended standard care for patients. The goal of pulmonary rehabilitation is to provide the patients a better quality of life. [51]

AIM & OBJECTIVE

AIM & OBJECTIVE

AIM

To analyze the pattern of lung damage – obstructive / restrictive / mixed whichever is commonly occurring in Pulmonary Tuberculosis sequelae patients

OBJECTIVE

1) To find the association between **Number of Episodes of TB Treatment** and pattern of lung damage thereafter.
2) To find the association between **Lag Time** (time interval between onset of symptoms and diagnosis of the disease) and extent of destruction of lung tissue.
3) To assess the progression of damage of lung tissue and its association with Time **Duration After Completion of Treatment**

MATERIAL AND METHODS

MATERIAL & METHODOLOGY

DESIGN OF STUDY

Cross – sectional study

MATERIAL

120 patients both male & female (male-81 and female – 39) attending Thoracic Medicine outpatient department at Chengalpattu Medical College were selected for the study.

INCLUSION CRITERIA

1) Both male & female
2) Age 30 -60 years
3) Released from treatment 18 months prior to the study and within 5years after completion of treatment.
4) Cessation of smoking after diagnosis of Pulmonary TB

EXCLUSION CRITERIA

1) Active pulmonary TB
2) Extra pulmonary TB
3) MDR TB
4) HIV positive
5) Severe respiratory distress

6) Bed ridden

7) Pregnancy

8) Diabetes mellitus

9) Recent myocardial infarction

10) Cardiac disease like unstable angina

11) Connective tissue disease

12) Post thoracic surgery

13) Chest / abdominal pain /oral / facial pain of any cause

MATERIAL

Easy On PC Spirometry (ndd medizintechnik AG, Zurich, Switzerland)

Working principle is the Ultrasound flow sensor measures the transit time which allows the accurate determination of flow velocity independent of temperature, humidity and molar mass of the gas. Since the measuring principle is based on a digital measurement technique the sensor requires only one single calibration and does not change during the sensor's lifetime.

METHODOLGY

Precautions

1) 2 sputum samples were taken prior to procedure and sputum negativity was confirmed by Zeihl-Neelson technique.

2) Chest X-ray PA view taken

3) Random blood sugar to rule out diabetes mellitus was taken

4) ELISA for HIV done and results verified

5) Institutional Ethics committee approval was obtained.

ON THE DAY OF RECORDING

Subject was advised to avoid

1) Full meals 2 hours prior to the test

2) Alcohol consumption 4 hours prior to the test.

3) Short acting bronchodilators 6 hours prior to the test

4) Long acting bronchodilators 12 hours prior to the test

5) Switch off the mobile phone

PROCEDURE

Informed consent was obtained

Anthropometric measurements - Height and weight of the subject was measured.

SPIROGRAM (OPEN CIRCUIT METHOD)

- Subject was seated comfortable and relaxed in an armed chair with straight back
- Procedure demonstrated by the investigator
- Subject was asked to inhale air deeply to fill the lungs

- ❖ Nose clip is placed immediately
- ❖ Spirette is kept inside the mouth of the patient with lips tightly sealing around the spirette
- ❖ Subject is asked to blow out air as fast and as hard as possible i.e., BLAST OUT for a minimum of 6 seconds
- ❖ Likewise, minimum of 3 trials done with an interval of 5 minutes in between each trial
- ❖ Best of three trials taken for analysis [21]

FLOW VOLUME LOOP (OPEN CIRCUIT METHOD)

- ❖ Ask the subject to sit comfortably and relaxed in an armed chair with straight back
- ❖ Procedure demonstrated to the subject
- ❖ Subject is asked to inhale atmospheric air deeply
- ❖ Nose clip is placed immediately
- ❖ Spirette is kept inside the mouth with lips tightly sealed around it
- ❖ The subject is asked to blow out air as fast and as hard as possible, BLAST OUT for a minimum of 6 seconds
- ❖ Then immediately ask the subject to inhale deeply with the spirette still inside the mouth (to form a loop)

- ❖ Minimum of 3 trials done with an interval of 5 minutes between each trial
- ❖ Best of 3 trials taken for analysis [21]

ACCEPTABILITY CRITERIA:

According to American Thoracic Society Criteria

- Effort should be maximal, smooth and cough free
- Exhalation time should be for a minimum of 6 seconds
- End of test is indicated by 2-second volume plateau [24, 25]

REPRODUCIBILITY CRITERIA:

According to American Thoracic Society Criteria

- Two largest FVC measurements should be within 200ml of each other
- Two largest FEV_1 measurements should be within 200ml of each other[24,25]

ANALYSIS:

Percentage of the Predicted values of FEV_1, FVC, FEV_1 / FVC, $FEF_{25\% -75\%}$ were taken for analysis.

The pattern of lung function impairment was assessed from spirometry results using percentage of the predicted values of FEV_1/FVC, FVC. [25]

Severity of restrictive impairment of lung function was assessed using percentage of predicted values of FVC. [26]

SEVERITY OF RESTRICTIVE PATERN

(BASED ON FVC %)

Mild restriction – 60 to 80%

Moderate restriction – 45 to 59%

Severe restriction - <45% [25,26]

Statistical analysis was done by using SPSS 16.0 version.

RESULTS

RESULTS

120 subjects (male -81, female – 39) who had completed tuberculosis treatment 18 months before the study and within 5 years of completion of treatment were participated in the study.

The following patterns of lung function impairment were obtained by spirometry.

1) Mild restriction pattern

2) Moderate restriction pattern

3) Severe restriction pattern

4) Mixed pattern

5) Few had normal study pattern also (13 subjects)

Anthropometric measurements and lung function parameters were analysed by arithmetic mean and standard deviation.

The mean value of lung function parameters in each pattern of lung function impairment was analysed by ANOVA and Chi square test.

The mean value of lung function parameters were correlated with number of episodes of TB treatment, time duration after treatment (months) and lag time in days (time duration between onset of symptom and diagnosis) by Spearman's rho analysis.

TABLE II

Descriptive Statistics

Parameter	Min	Max	Mean ± S.D
Age	30	60	48 ± 9.2
Height	139	176	157 ± 8.41
Weight	35	70	52.9 ± 9.92
BMI	12.6	34.7	21.55 ± 4.34
FVC (Percentage of predicted value)	25	99	57.15 ± 16.46
FEV_1 (Percentage of predicted value)	16	96	57.27 ± 19.39
FEV_1/FVC (Percentage of predicted value)	46	120.45	89.09 ± 15.71
$FEF_{25-75\%}$ (Percentage of predicted value)	7	120	41.32 ± 25.97

The above table shows baseline data of study group.

Anthropometric measurements and Lung function parameters were analysed by Arithmetic Mean and Standard Deviation.

TABLE III

Frequency percent distribution of age group

Age	Frequency	Percent
30-40	32	26.6
41-50	35	29.2
51-60	53	44.2
Total	120	100

Maximum number of patients belongs to age group 51 – 60.

Minimum number of patients belongs to age group 30 – 40.

Figure 6: Frequency percent distribution of age group

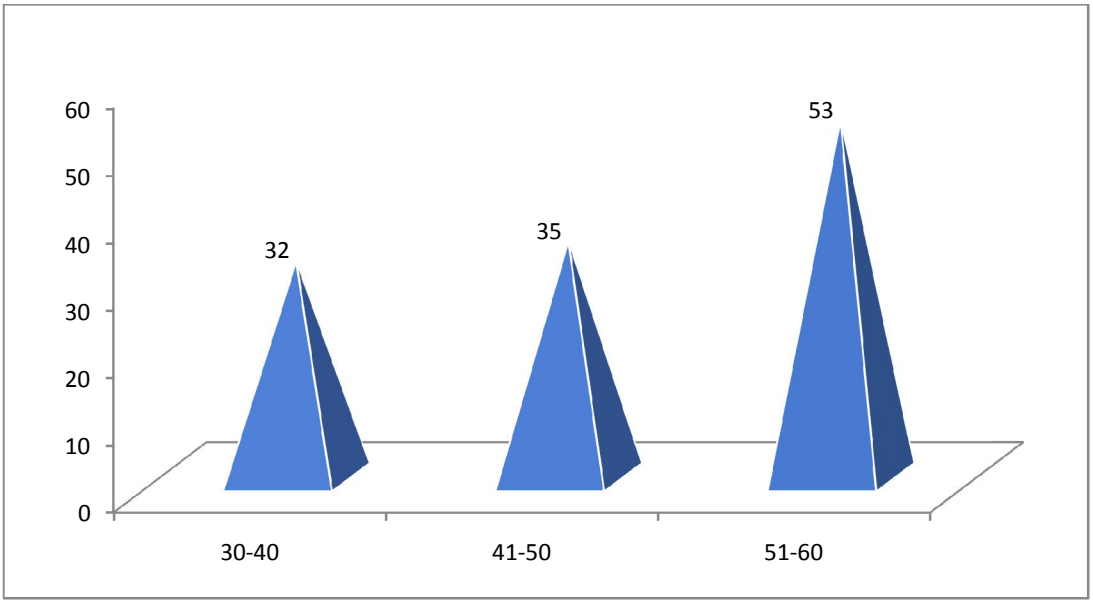


TABLE IV

Frequency percentage of Gender distribution of study group

SEX	Frequency	Percent
Male	81	67.5
Female	39	32.5
Total	120	100

Among the 120 subjects participated in this study 67.5% were male subjects, and 32.5% were female subjects.

Male : female ratio in this study was around 2:1

Figure 7: Frequency percentage of Gender distribution of study group

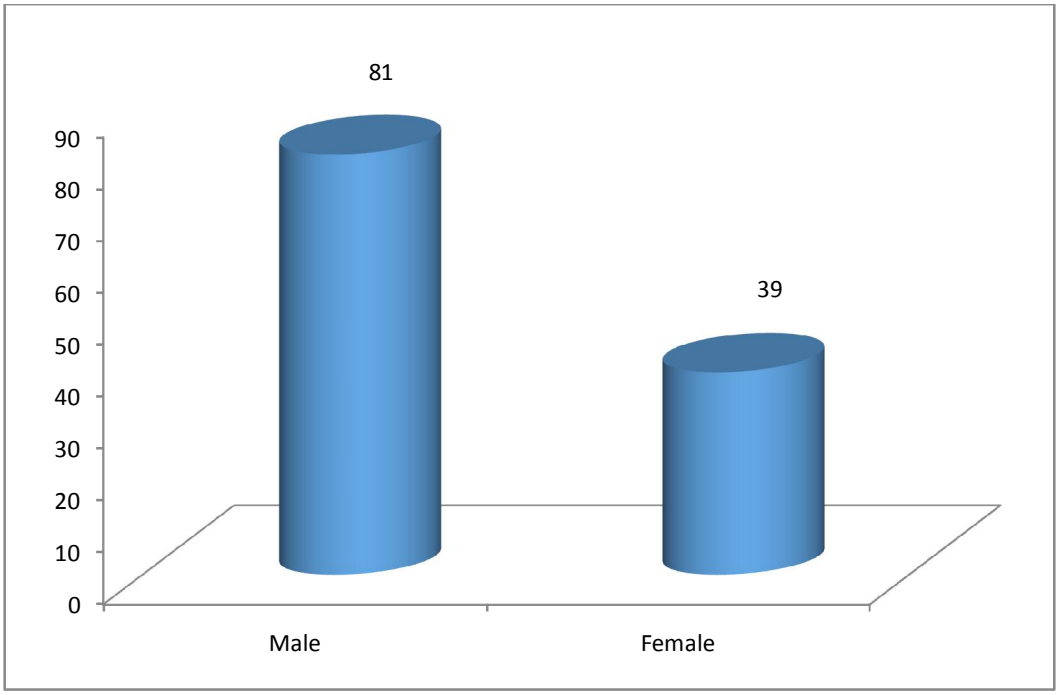


TABLE V

Frequency distribution of different patterns of Lung Function Impairment.

Diagnosis	Frequency (n=120)	Percent (100)
Mild restriction	40	33.3
Moderate restriction	32	26.7
Severe restriction	14	11.7
Mixed pattern	21	17.5
Normal study	13	10.8

This table shows the distribution of pattern of Lung Function Impairment among the study group.

Figure 8: Frequency distribution of different patterns of Lung Function Impairment

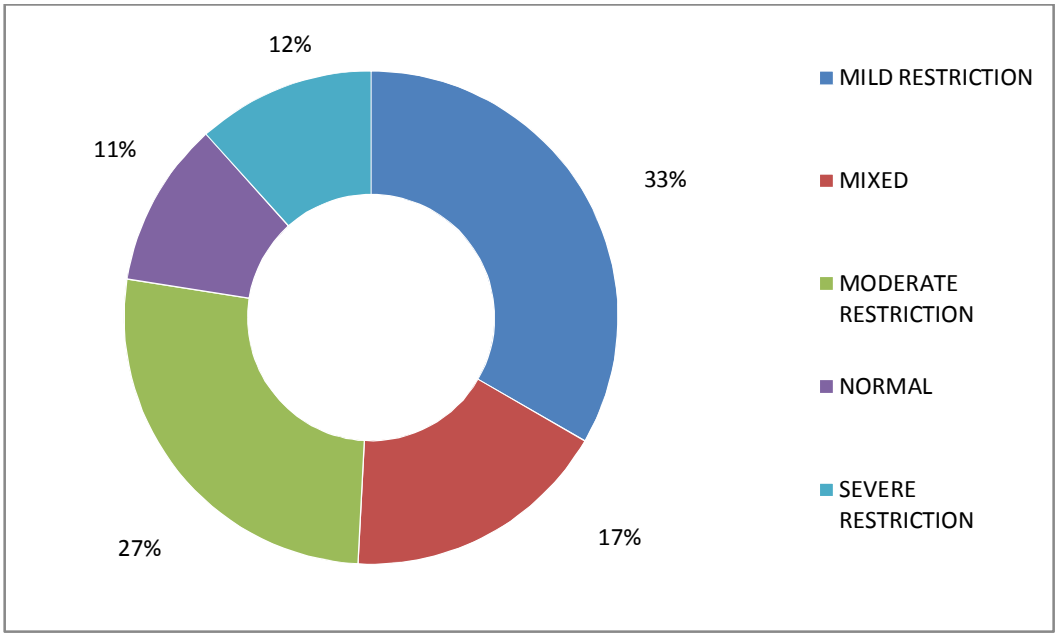


TABLE VI

FVC in various patterns of Lung Function Impairment

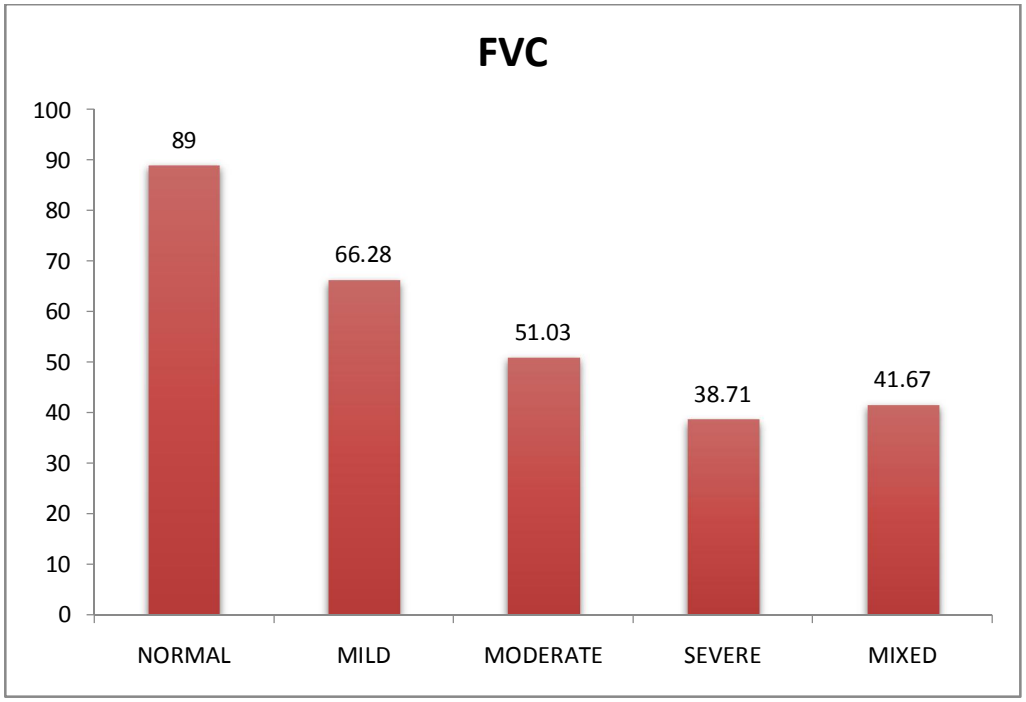
Parameters	Pattern of damage	N	Mean ± S.D	Minimum	Maximum	F	Sig
FVC (Percentage of predicted value)	Normal study	13	89 ± 6.04	80	99	166.49	**0.000***
	Mild restriction	40	66.28 ± 5.27	60	80		
	Moderate restriction	32	51.03 ± 5.91	26	59		
	Severe restriction	14	38.71 ± 3.81	34	45		
	Mixed pattern	21	41.67 ± 9.90	25	62		
	Total	120	57.15 ± 16.47	25	99		

Mean ± S.D value of FVC varies significantly in different patterns of lung function study **(P < 0.01)**.

FVC value decreases as severity of lung impairment increases

Statistical analysis was done by **ANOVA**.

Figure 9: FVC in various patterns of Lung Function Impairment.



Significant difference in mean value of FVC between normal study and restrictive pattern was observed.

There is significant decrease in mean FVC value between mild restriction and severe restriction pattern of lung damage.

There is not much difference between mean value of FVC in mixed pattern and mean value of FVC in severe restriction.

TABLE VII

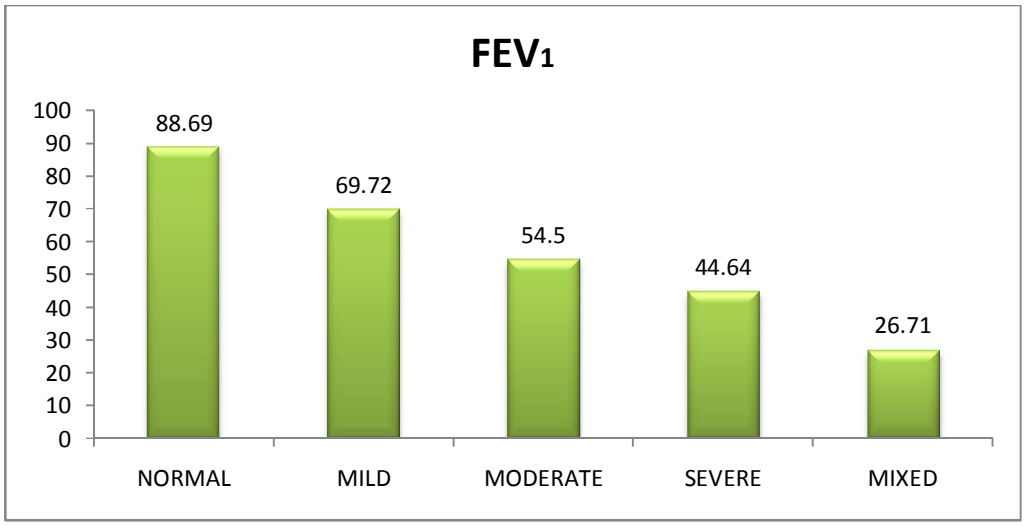
FEV_1 in various patterns of Lung Function Impairment

Parameter	Pattern of damage	N	Mean ± S.D	Minimum	Maximum	F	Sig
FEV_1 (Percentage of predicted value)	Normal study	13	88.69 ± 5.00	81	96	326.78	**0.000***
	Mild restriction	40	69.72 ± 4.52	60	83		
	Moderate restriction	32	54.5 ± 6.79	43	66		
	Severe restriction	14	44.64 ± 4.10	35	51		
	Mixed pattern	21	26.71 ± 6.61	16	37		
	Total	120	57.27 ± 19.40	16	96		

Statistical analysis by ANOVA shows that the Mean ± S.D value of FEV_1 varies significantly in different patterns of lung function study **($P < 0.01$)**.

FEV_1 value decreases as severity of restrictive pattern increases, but mean value of FEV_1 is higher compared to FVC in restrictive patterns of lung impairment except in mixed pattern.

Figure 10: FEV_1 in various patterns of Lung Function Impairment



The difference in mean value of FEV_1 between normal study and restrictive pattern is much less compared to difference in mean value of FVC between normal study and restrictive pattern.

Significant decrease in FEV_1 Value was observed as severity of lung damage increases.

Significant difference in mean value of FEV_1 between restrictive pattern and mixed pattern was observed.

TABLE VIII

FEV_1 / FVC in various patterns of Lung Function Impairment

Parameter	Pattern of damage	N	Mean ± S.D	Minimum	Maximum	F	Sig
FEV_1 / FVC (Percentage of predicted value)	Normal study	13	99.92 ± 6.37	90	111	47.33	**0.000***
	Mild restriction	40	95.24 ± 7.51	81.58	113.33		
	Moderate restriction	32	94.84 ± 15.14	50.98	120.45		
	Severe restriction	14	87.29 ± 6.67	76	97		
	Mixed pattern	21	63.14 ± 6.05	46	71		
	Total	120	89.10 ± 15.71	46	120.45		

Statistically significant **(P < 0.01)** variation was noted in FEV_1 / FVC values depending up on the severity of lung damage.

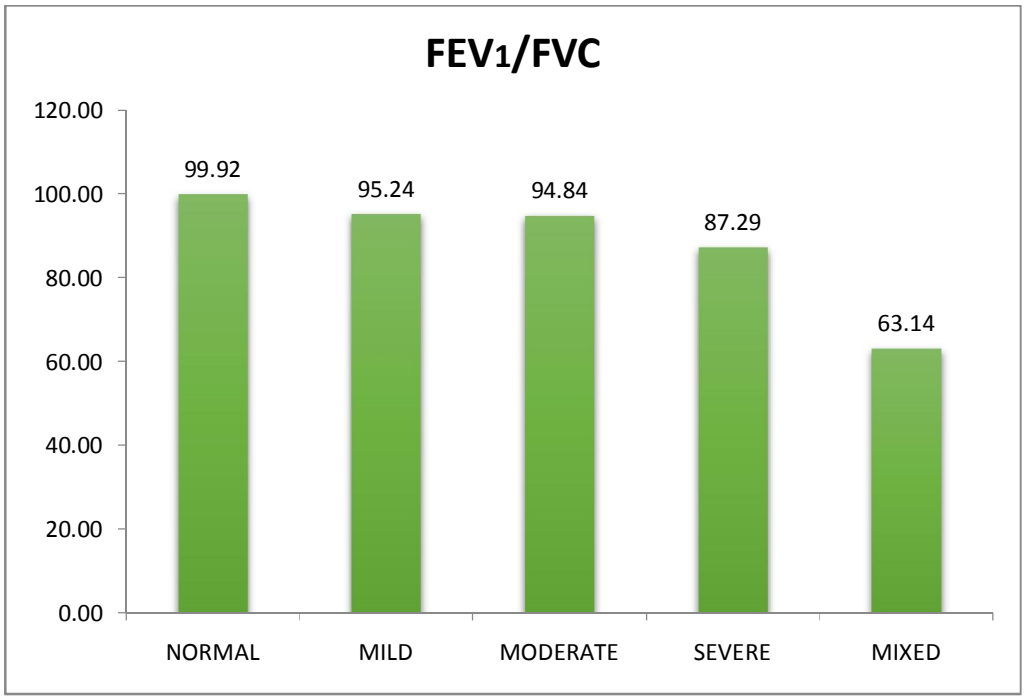
As severity increases the mean value of FEV_1 / FVC decreases.

But in all range of severity value of FEV_1 / FVC is >70% suggesting that the pattern of damage was restrictive in nature.

In mixed pattern mean FEV_1/FVC is less than 70%

ANOVA test was used for analysis.

Figure 11: FEV_1 / FVC in various patterns of Lung Function Impairment



Mean FEV_1/FVC value is more than 70% indicating the pattern of damage is restrictive, but significant decrease in mean value was observed as severity increases.

In mixed pattern the FEV_1/FVC is below 70%.

TABLE IX

Comparison of mean ± S.D Values of FVC, FEV_1 and FEV_1/FVC between different patterns of Lung Function Impairment

Parameters (Percentage of predicted value)	Mild Restriction	Moderate Restriction	Severe Restriction	Mixed Pattern
FVC	66.28±5.27	51.03±5.91	38.71±3.81	41.67±9.90
FEV_1	69.72±4.52	54.5±6.79	44.64±4.10	26.71±6.61
FEV_1/FVC	95.24±7.51	94.84±15.14	87.29±6.67	63.14±6.05

Mean FVC is <80% and mean FEV_1/FVC <70% indicating the pattern of damage is restrictive.

As the severity of restriction increases value of both FVC and FEV_1/ FVC declines.

FEV_1 value is < 80% but decrease in FEV_1 is less compared to FVC.

In mixed pattern FVC, FEV_1, FEV_1/FVC values are below normal.

TABLE X

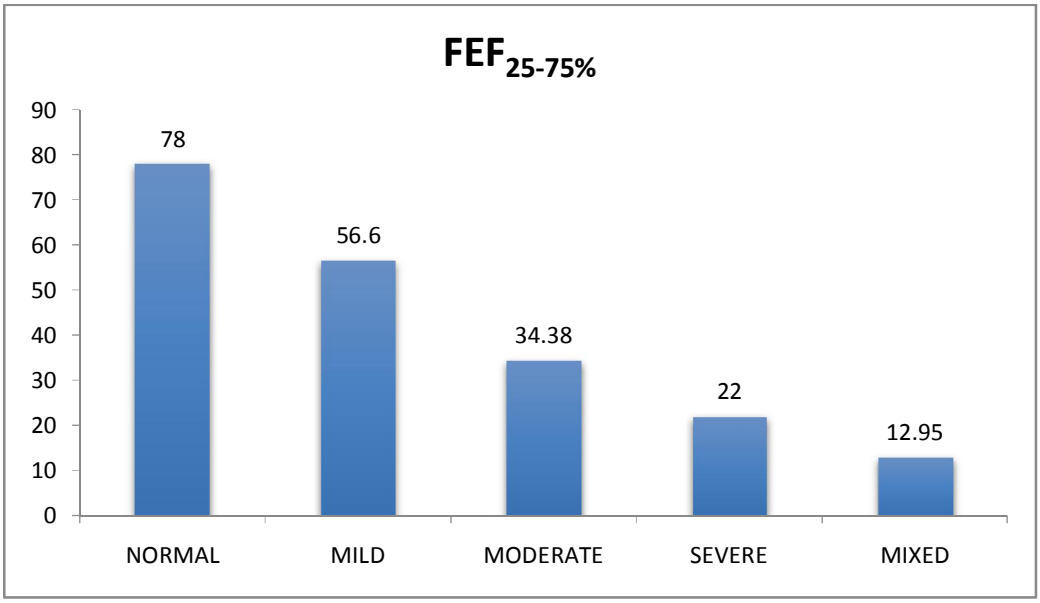
$FEF_{25-75\%}$ in various patterns of Lung Function Impairment

Parameter	Pattern of damage	N	Mean ± S.D	Minimum	Maximum	F	Sig
$FEF_{25-75\%}$ (Percentage of predicted value)	Normal Study	13	78 ± 16.85	51	111	48.75	**0.000***
	Mild restriction	40	56.6 ± 23.02	19	120		
	Moderate restriction	32	34.38 ± 12.67	20	73		
	Severe restriction	14	22 ± 6.06	11	32		
	Mixed pattern	21	12.95 ± 3.49	7	19		
	Total	120	41.32 ± 26.0	7	120		

Statistical analysis was done by ANOVA.

Significant difference **($P < 0.01$)** in $FEF_{25-75\%}$ value between different pattern of Lung Function Impairment was noted.

Figure 12: FEF $_{25\text{-}75\%}$ in various patterns of Lung Function Impairment



Mean value of FEF $_{25\text{-}75\%}$ in various patterns of Lung Function Impairment is well below 65% in restrictive and mixed pattern.

As severity of lung impairment increases mean value of FEF $_{25\text{-}75\%}$ decreases significantly.

Significant difference in mean value of FEF $_{25\text{-}75\%}$ between restrictive and mixed pattern was observed

TABLE XI

Relationship between Duration after Treatment and pattern of Lung Function Impairment

Parameter	Pattern of damage	N	Mean ± S.D	Minimum	Maximum	F	Sig
DURATION AFTER TREATMENT (MONTHS)	Normal study	13	43.15 ± 13.02	24	60	7.144	**0.000***
	Mild restriction	40	34.18 ± 11.0	18	60		
	Moderate restriction	32	37.12 ± 13.55	19	60		
	Severe restriction	14	41 ± 16.60	18	60		
	Mixed pattern	21	51.43 ± 10.25	24	60		
	Total	120	39.75 ± 13.79	18	60		

Statistically significant variation was seen between each pattern of damage and duration after treatment **(P<0.01)** .

As duration after treatment increases severity of lung function imapirment increases.

Few subjects (n=13) showed normal study as duration after treatment increases.

Analysis was done by ANOVA.

TABLE XII

Relationship between Lag time and pattern of Lung Function Impairment

Parameter	Pattern of damage	N	Mean ± S.D	Minimum	Maximum	F	Sig
Lag time (days)	Normal study	13	49.62 ± 15.47	30	75	39.22	**0.000***
	Mild restriction	40	60.75 ± 29.41	30	120		
	Moderate restriction	32	171.72 ± 95.34	30	365		
	Severe restriction	14	195 ± 72.30	60	330		
	Mixed pattern	21	254.76 ± 81.51	60	365		
	Total	120	138.75 ± 101.57	30	365		

ANOVA shows significant variation between each pattern of Lung Function Impairment and lag time **(P<0.01)** .

As lag time increases the lung function impairment is more severe.

TABLE XIII

Frequency distribution of Number of Episodes of Anti-TB treatment.

No. of Episode	Frequency (n=120)	Percent (100)
1	77	64.2
2	38	31.7
3	5	4.2

The above table shows higher percentage of subjects had taken single episode of Anti-TB treatment.

Figure 13 : Frequency distribution of Number of Episodes of Anti-TB Treatment.

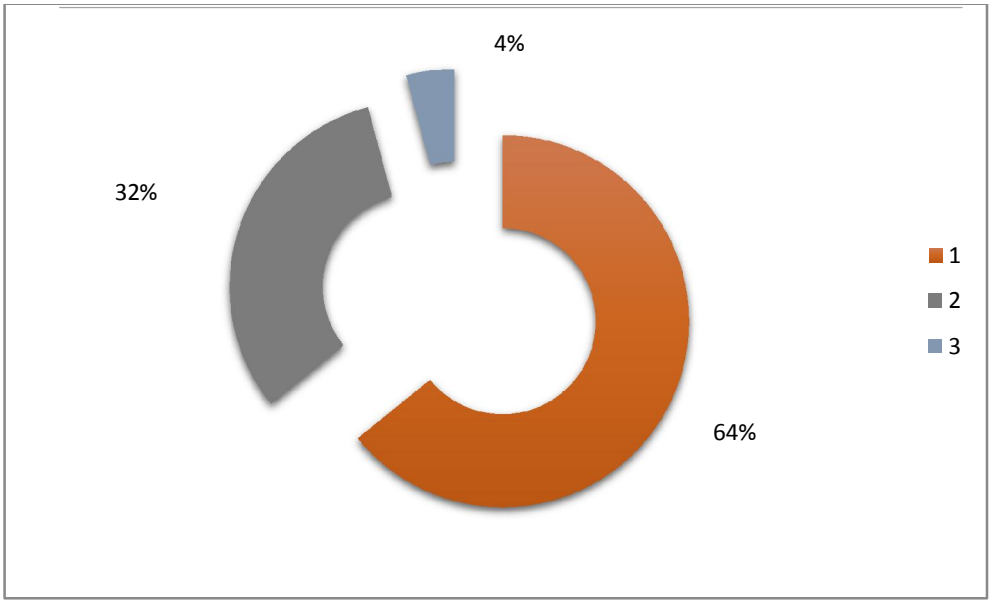


TABLE XIV

Relationship between No. of episodes of Anti-TB treatment and pattern of Lung Function Impairment

No Of Episodes	Normal Study	Mild Restriction	Moderate Restriction	Severe Restriction	Mixed Pattern	Total	Chi sq	P value
1	13	34	21	4	5	77	42.19	**0.000***
2	0	6	11	8	13	38		
3	0	0	0	2	3	5		
Total	13	40	32	14	21	120		

The table shows as number of episodes of Anti-TB treatment increases the severity of damage increases.

This was statistically analysed by chi square test.

P value is highly significant **(P<0.01)** .

TABLE XV

Correlation between FVC and No. of Episodes of Treatment, Duration after Treatment and Lag Time.

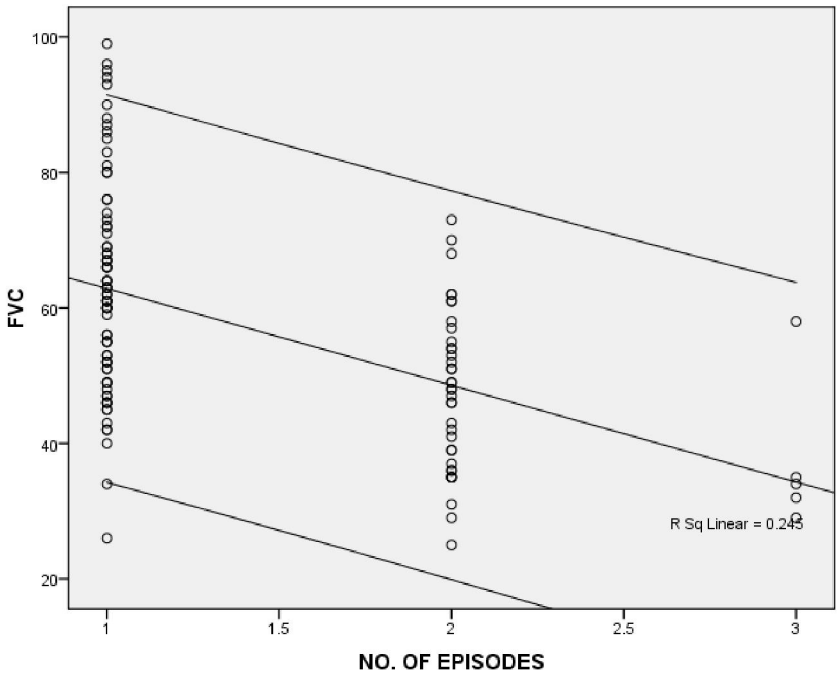
Parameter	Correlation	No. Of episodes	Duration after treatment	Lag time
FVC (Percentage of predicted value)	Correlation coefficient	-0.50	-0.90	-0.69
	Sig. (2-tailed)	**P=0.000***	**P=0.000***	**P=0.000***

Analysis done by Spearman's rho analysis..

Significant negative correlation between FVC,and No. of episodes of treatment , duration after treatment and lag time was found **(P<0.01)** .

Figure 14

Correlation between FVC and No. of Episodes of Treatment



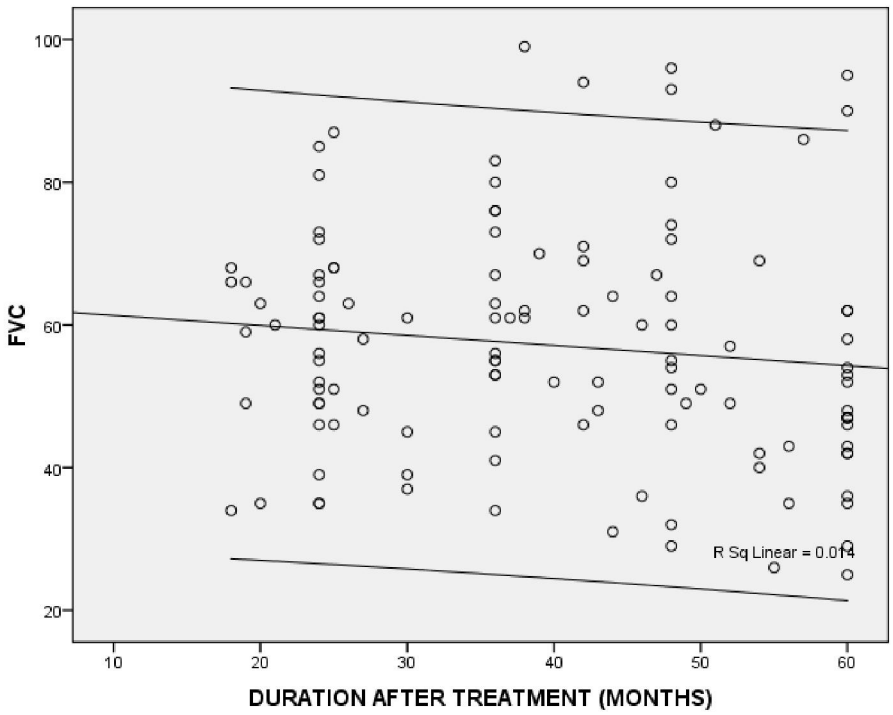
The centre line in the above scattered diagram indicates negative correlation was observed between FVC and number of episodes of treatment.

The lines above and below indicates confidence limit.

As number of episodes increase there is decrease in FVC value.

Figure 15

Correlation between FVC and Duration After Treatment



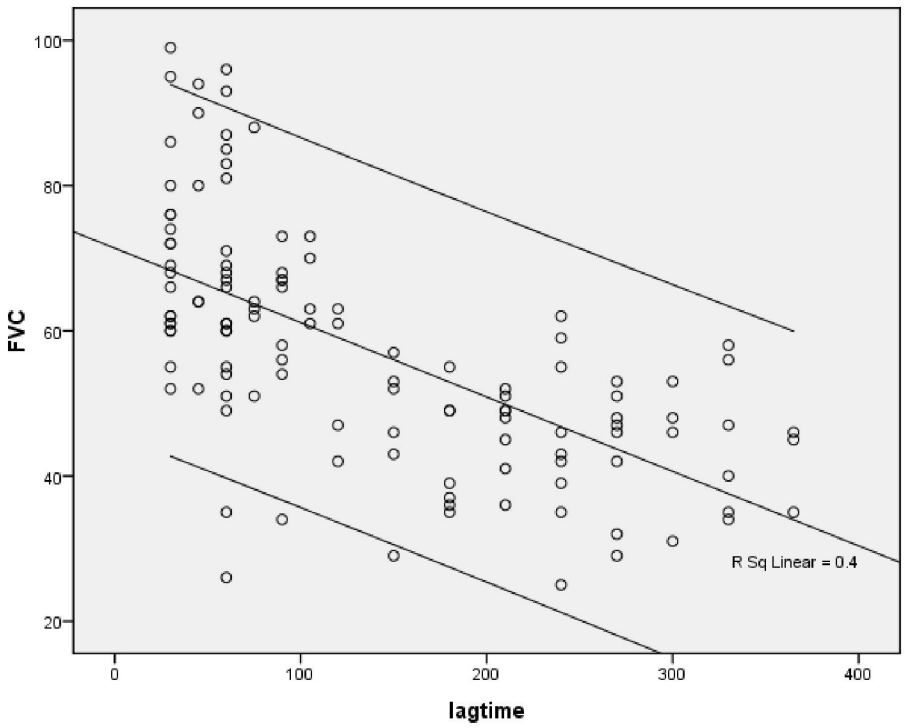
Centre line indicates negative correlation was observed between FVC and duration after treatment.

The distribution out of confidence limit is minimal.

FVC decreases as duration after treatment increases.

Figure 16

Correlation between FVC and Lag Time



Significant negative correlation was observed between FVC and lag time.

As time duration between onset of symptoms and diagnosis of tuberculosis increases there is significant decrease in FVC parameter.

The distribution of variable is clustered around centre line.

TABLE XVI

Correlation between FEV_1 and No. of Episodes of Treatment, Duration After Treatment And Lag Time

Parameter	Correlation	No. Of episodes	Duration after treatment	Lag time
FEV_1 (Percentage of predicted value)	Correlation coefficient	-52	-0.95	-0.71
	Sig. (2-tailed)	**P=0.000***	**P=0.000***	**P=0.000***

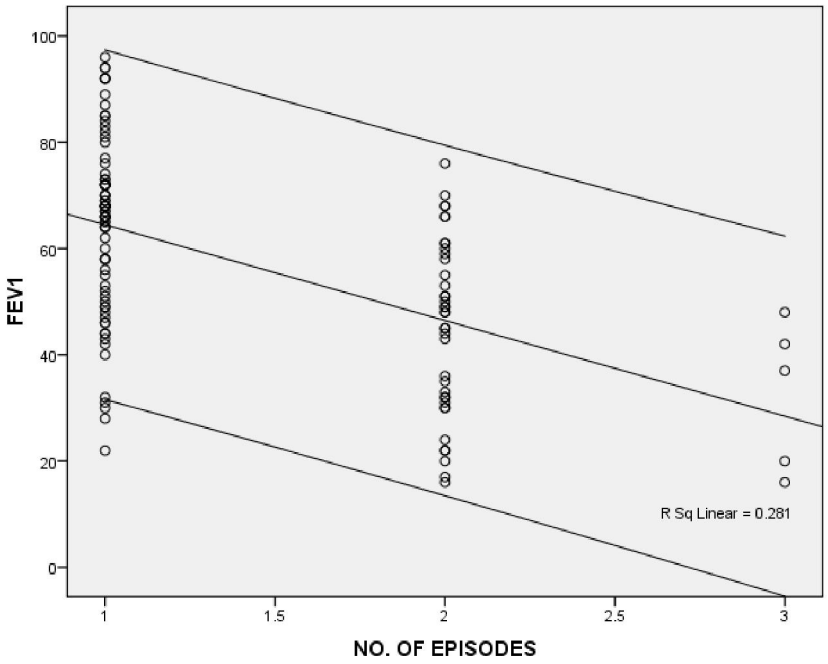
Negative correlation between FEV_1 and No. of episodes of treatment, duration after treatment and lag time was found.

Correlation was significant **(P<0.01)** .

Analysis done by Spearman's rho analysis.

Figure 17

Correlation between FEV_1 and No. of Episodes of Treatment.

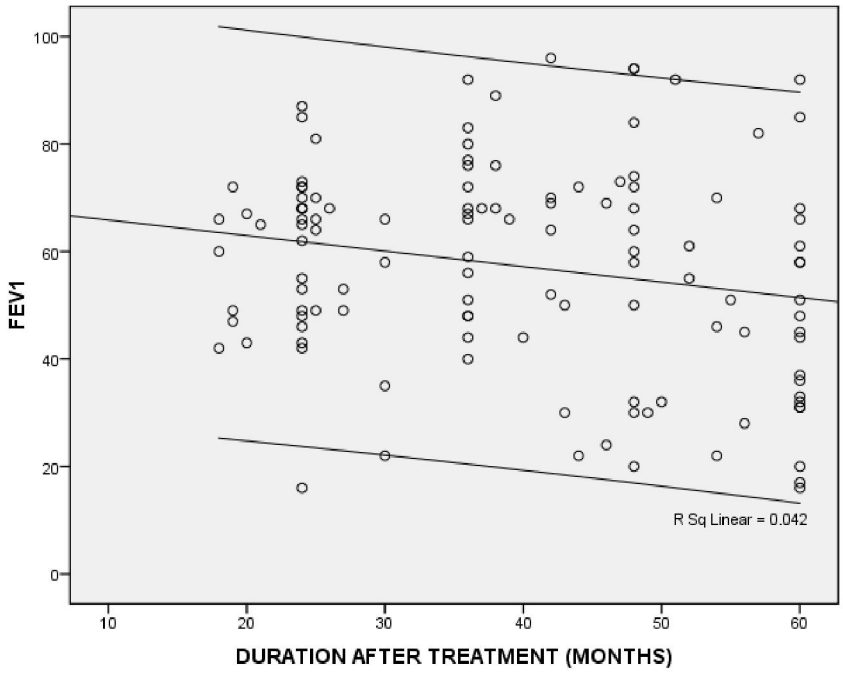


Negative correlation was observed between FEV_1 and number of epidoses of anti-TB treatment.

Higher percentage os subjects had taken single episode of of anti-TB treatment.

Figure 18

Correlation between FEV_1 and Duration After Treatment .

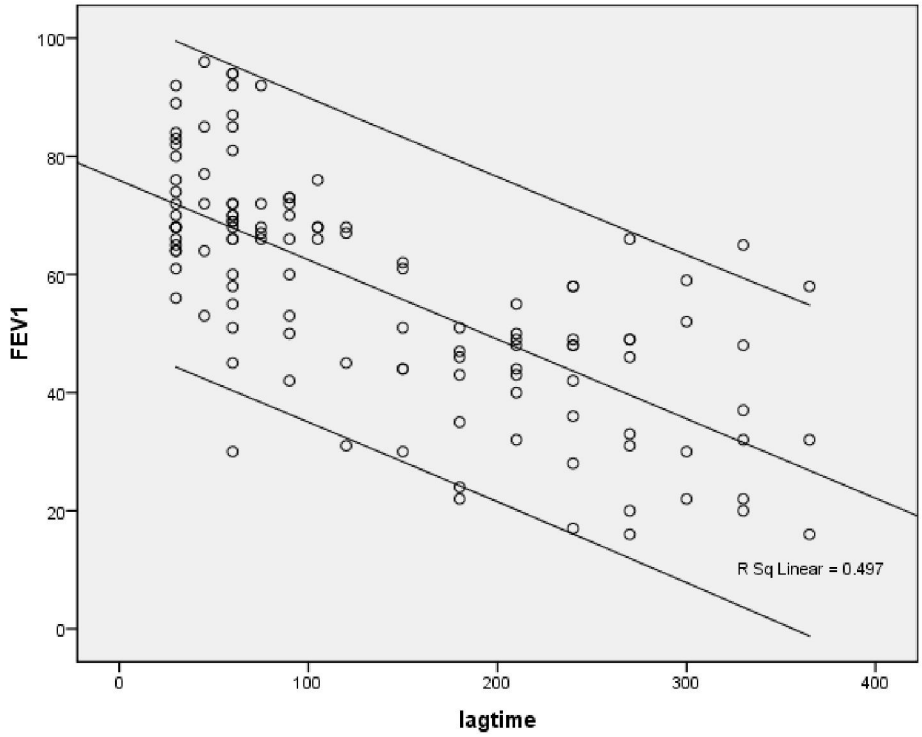


Negative correlation was observed between FEV_1 and duration after completion of Anti-TB treatment.

The negative correlation is less compared to number of episodes of treatment.

Figure 19

Correlation between FEV_1 and Lag Time



Negative correlation was observed between FEV_1 and lag time.

As lag time increases there is decrease in FEV_1 parameter.

Distribution outside the confidence limit is minimal.

TABLE XVII

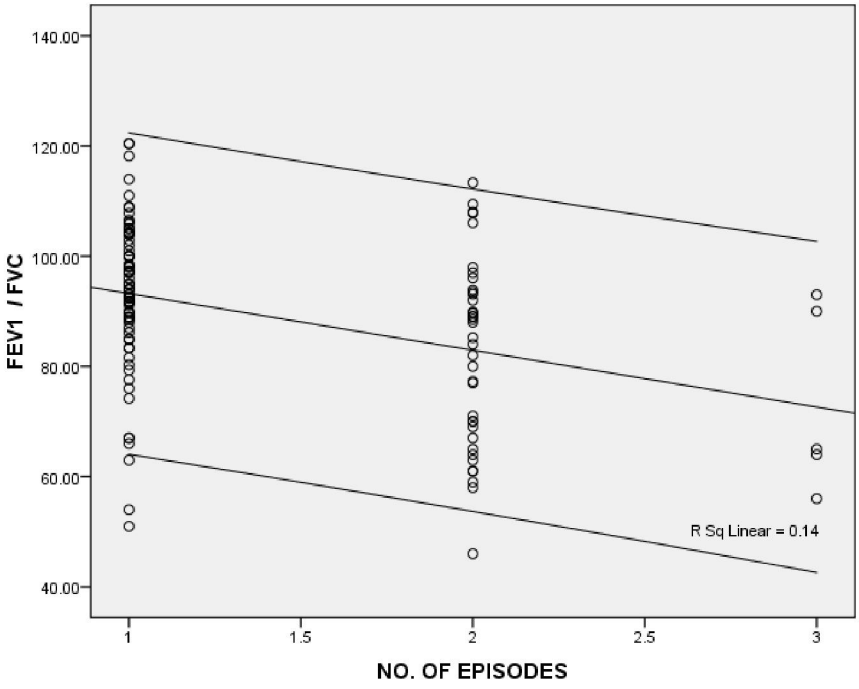
Correlation between FEV_1 / FVC and No. of Episodes of Treatment, Duration After Treatment and Lag Time

Parameter	Correlation	No. Of episodes	Duration after treatment	Lag time
FEV_1 / FVC (percentage of predicted value)	Correlation coefficient	-0.35	-0.61	-0.403
	Sig. (2-tailed)	**P=0.000***	**P=0.000***	**P=0.000***

Spearman's rho analysis shows there is significant negative correlation between FEV_1 / FVC and No. of Episodes of Treatment, Duration After Treatment and Lag Time **(P<0.01)**.

Figure 20

Correlation between FEV_1 / FVC and No. of Episodes of Treatment.

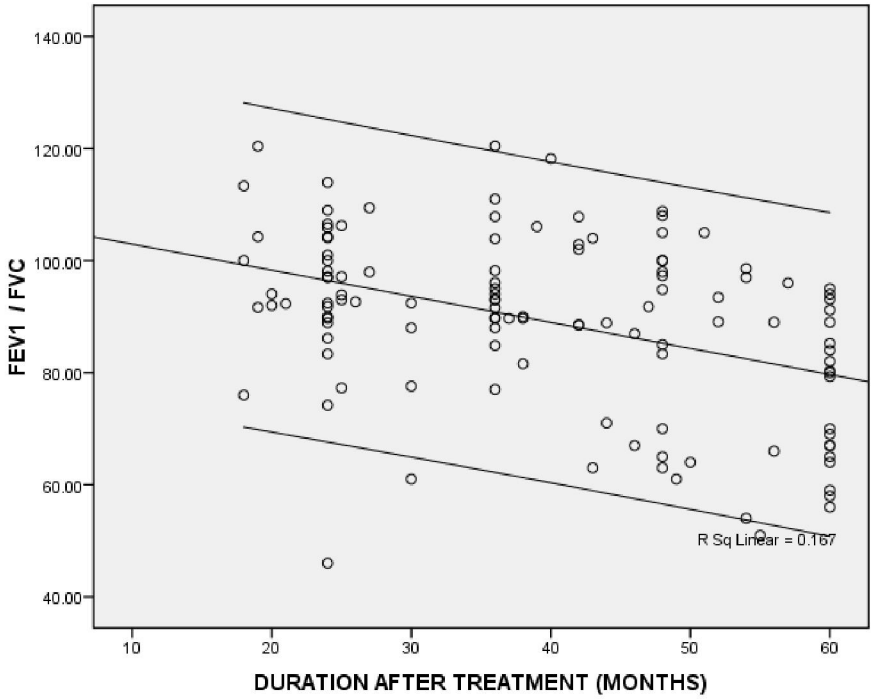


Negative correlation was observed between FEV_1 / FVC and number of epidoses of anti-TB treatment.

Correlation line is less steep compared to correlation between FVC , FEV_1 and number of episodes of anti-TB treatment.

Figure 21

Correlation between FEV_1 / FVC and Duration After Treatment.

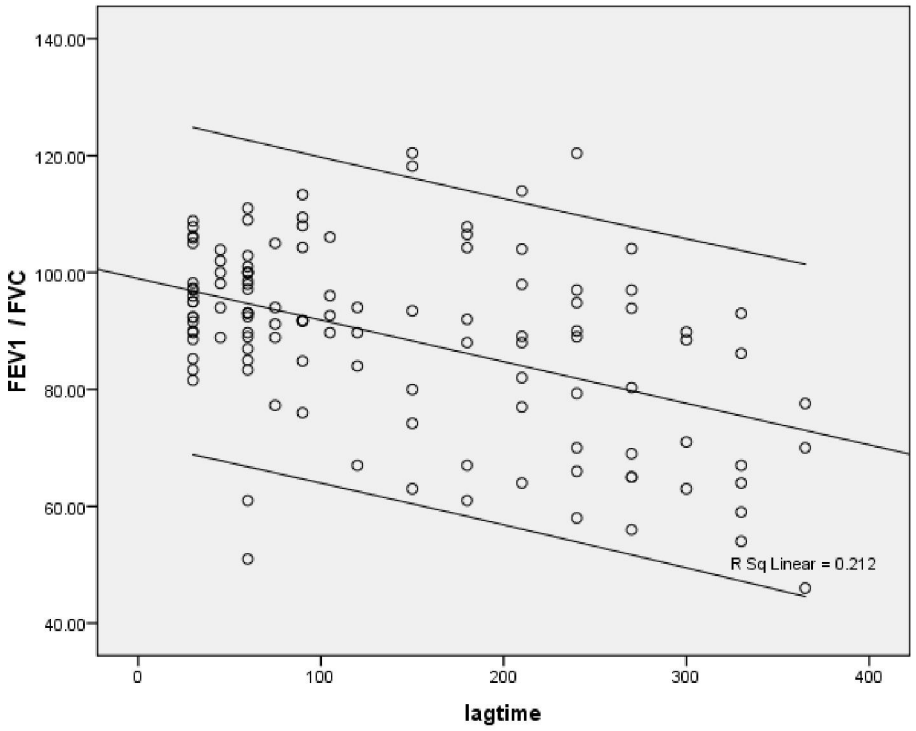


Negative correlation was observed between FEV_1 / FVC and duration after Anti-TB treatment.

Distribution is not much clustered around centre line as in FVC and FEV_1.

Figure 22

Correlation between FEV_1 / FVC and Lag Time



Negative correlation was observed between FEV_1 / FVC and lag time.

Distribution outside confidence limit is minimal.

TABLE XVIII

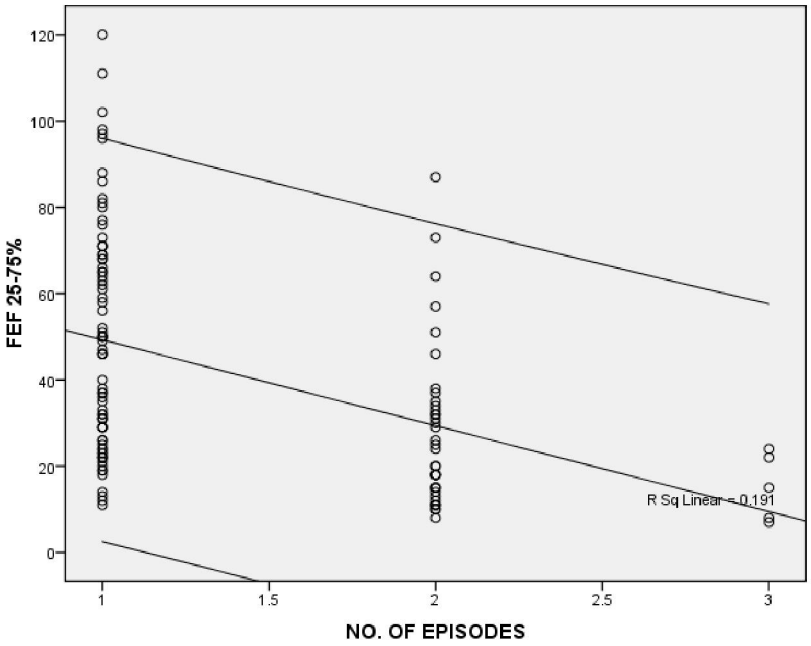
Correlation between $FEF_{25-75\%}$ and No. of Episodes of Treatment, Duration After Treatment And Lag Time .

Parameter	Correlation	No. Of episodes	Duration after treatment	Lag time
$FEF_{25-75\%}$ (Percentage of predicted value)	Correlation coefficient	-0.48	-0.85	-0.66
	Sig. (2-tailed)	**P=0.000***	**P=0.000***	**P=0.000***

Spearman's rho analysis shows there is significant negative correlation between $FEF_{25-75\%}$ and No. of Episodes of Treatment, Duration After Treatment and Lag Time **(P<0.01)** .

Figure 23

Correlation between FEF $_{25\text{-}75\%}$ and No. of Episodes of Treatment

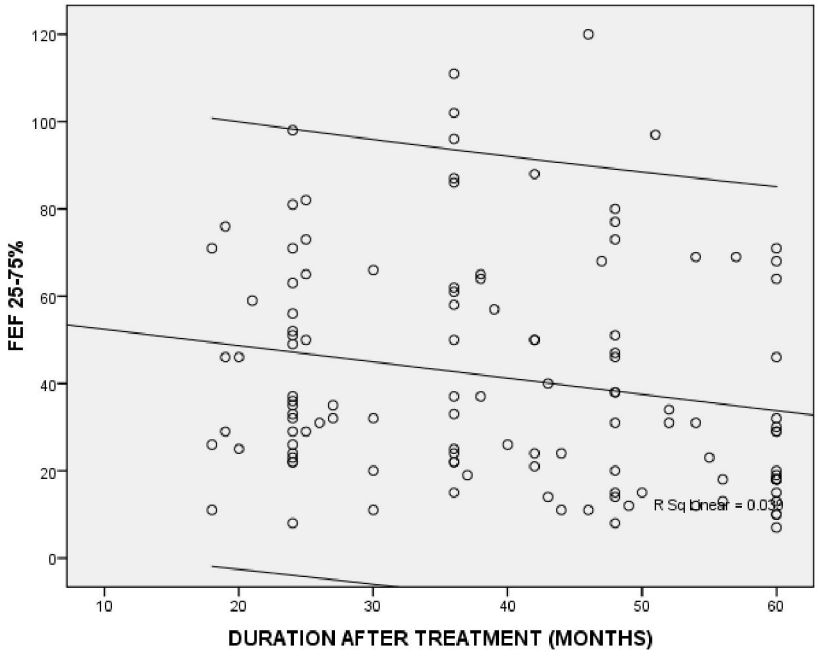


Negative correlation was observed between FEF $_{25\text{-}75\%}$ and number of epidoses of Anti-TB treatment.

Higher percentage of subjects had taken single episode of of anti-TB treatment.

Figure 24

Correlation between FEF $_{25\text{-}75\%}$ and Duration After Treatment

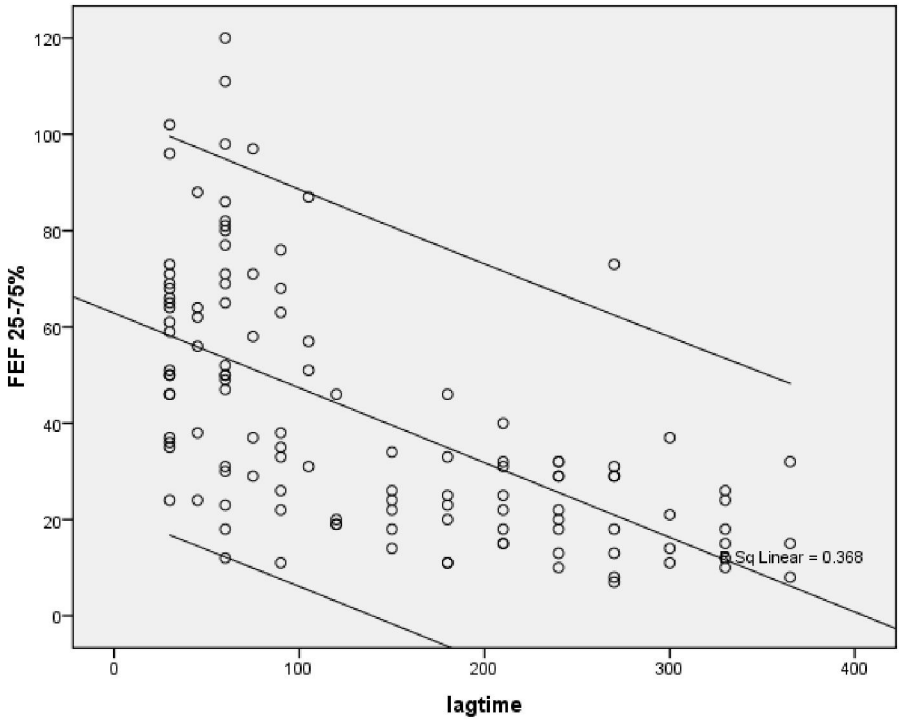


Negative correlation was observed between FEF $_{25\text{-}75\%}$ and duration after Anti-TB treatment.

Distribution is much less clustered around centre line but distribution outside confidence limit is minimal.

Figure 25

Correlation between FEF $_{25\text{-}75\%}$ and Lag Time



Negative correlation was observed between FEF $_{25\text{-}75\%}$ and lag time.

Distribution is more clustered around centre line but distribution outside confidence limit is minimal.

DISCUSSION

DISCUSSION

Tuberculosis is a worldwide public health problem with higher morbidity and mortality among all chronic infections. India alone accounts for 24% of global burden of Tuberculosis. [2]

Pulmonary Tuberculosis affects almost all parts of the respiratory system including bronchi, bronchioles, lung parenchyma and lymph nodes. The pathogenesis involved is an inflammatory process causing upregulation of several proteases like matrix metalloproteinases and dysregulation of protease control which causes lung remodeling [3]

Histopathological abnormalities occur even after successful treatment of the disease causing sequelae changes in the lungs which can be in the form of fibrosis, cavity formation, bronchial and bronchiolar obstruction, bronchiectasis etc. These sequelae changes in the respiratory tract can cause obstructive, restrictive or mixed pattern of lung function impairment. [3]

Many studies have shown that the common pattern of lung function impairment in pulmonary TB sequelae patients was obstructive in nature. But the recent studies have shown that restrictive pattern and mixed pattern are most commonly observed rather than obstructive pattern in these patients. [3]

All these changes result in abnormal gas exchange which not only affects the respiratory system but indirectly leads to frequent comorbidities in post treatment

period. Dysfunction involving other systems like cardiovascular system, skeletal muscles is common in post tuberculosis treatment period. [53]

All these factors have a negative effect on quality of life of a patient who had been treated for tuberculosis with successful therapy, so it is essential to assess the impairment of lung function as early as possible for an early intervention. [55, 58]

In the present study the age group of selected subjects was between 30 – 60 years but it was observed that more number of patients fall in the age group of 51 - 60 years (44%) compared to 26% who belonged to age group 30-40 years. This may be because normally there is gradual decline in pulmonary function after the age of 30 years. [25] In Tuberculosis affected elderly individual there is an accelerated decline of lung function noticed especially over the age of 40. [54]

More number of male patients participated in the present study compared to female patients (Male-81, Female-39). There is evidence in global TB report 2014 which states that 60% of new cases reported every year belong to male gender. [2]

The gender difference is may be due to the fact that less number of women approaches for medical aid compared to men. The other factors contributing to increased susceptibility to TB infection in male gender are the habit of tobacco use either by smoking, tobacco quid is common among them and also the risk of exposure to the infection and passive smoking in working environment is more for men compared to women.

In the present study, smoking was not discussed as a significant predictor for lung function impairment because all the males who participated in the study had

quitted smoking just after the diagnosis of pulmonary tuberculosis and none of the women had a history of smoking before and after the attack of Tuberculosis.

PATTERN OF LUNG FUNCTION IMPAIRMENT

The pattern of lung function impairment observed in the study were restrictive pattern and mixed pattern only. The probable reason for this may be the increase in lag time period i.e. the time duration between onset of respiratory symptoms and the time of diagnosis as Tuberculosis.

There is concrete evidence that as the lag time increases the extent of damage to lung also increases. [48] The Lag time in this study varies from a minimum of 30 days to maximum of 365 days. This may be because most of the patients are asymptomatic or may experience minimal symptoms like fever and malaise ordinarily until disease is far advanced especially during primary Tuberculosisi. [47] Another cause may be the subjects participated in the study were from rural areas with poor health education and poor socioeconomic status which hampers them to access medical aid as early as they experienced symptoms. This increased Lag time might have been the cause for extensive damage resulting in restrictive or mixed pattern.

Few subjects in the study (13 out of 120) had a normal pattern in spirometry. This may be due to different factors such as they might have had better pulmonary function prior to attack of tuberculosis compared to subjects who showed restrictive/mixed pattern. The occupational and environmental exposure might have been less compared to other subjects.

According to Mohammed Saleh Al- Hajjaj a continuous healing process is taking place in the lungs even after completion of treatment. This may also be the cause for normal study in these patients. [54]

FEV_1/FVC RATIO

The ratio in all types of impairment is well above 70% suggesting the pattern of damage is restrictive in nature. The severity of restrictive pattern of damage was assessed based on FVC value. [25] Accordingly, the severity varied from mild to moderate to severe restriction in the present study

And also it was observed that there is decline in FVC & FEV_1 values depending upon the severity of lung impairment. This is in consistent with a study by Luiz Carlos D'Aquino et al who says that interpretation of restrictive pattern identified by Spirometry can be made more accurate by incorporating the magnitude of reduction in FVC and elevated FEV_1/FVC ratio. [46]

FVC & FEV_1

In the present study a significant decrease in FVC & FEV_1 was noted as severity of restriction increases. Decline in FVC value was more compared to decline in FEV_1. This is in consistent with a study by Eun Jo Lee et al who found that there is negative correlation between FVC and FEV_1 values and extent of Lung damage. [56]

Venkateshiah et al in their study had also stated the usefulness of both FVC & FEV_1 values in evaluating the extent of destruction of lung. According to them the FVC and FEV_1 decline as severity of damage increase. [47]

In mixed pattern where both obstructive and restrictive damage occurs and there is significant decrease in FVC and FEV_1. and the value of FEV_1/FVC is around 63% which is well below 70%. [25]

FEF $_{25-75\%}$

The decline in value of FEF $_{25-75\%}$ below 65% in both restrictive and mixed pattern of damage in this study indicates there was significant smaller airway obstruction in these subjects. This is consistent with finding of Eric Walter Pefura-Yone et al who suggest that FEF $_{25-75\%}$ <65% is a useful criterion for diagnosis of small airway obstruction in treated pulmonary TB patients who had restrictive /mixed pattern. They also suggested that decrease in FEF $_{25-75\%}$ is associated with poor profile of other spirometry indices like FVC & FEV_1. This was also observed in the present study. [48]

The pathogenesis of small airway obstruction is due to destruction of parenchyma surrounding the distal small airways by fibrosis causes the loss of radial traction on the airways thereby causing distortion and narrowing of these small airways. [48]

DURATION AFTER TREATMENT AND LUNG FUNCTION IMPAIRMENT

In the present study there was negative correlation between pulmonary function parameters and duration after treatment. There is controversial evidence in studies regarding the relationship between duration after completion of treatment and decline of lung function.

Some studies say that the nadir of pulmonary function impairment occurs at around 18 months after completion of treatment and as duration after treatment increases thereafter the severity of damage also increases. [3]. Vargha .G also confirms this in a fifteen year follow up study on both obstructive and non- obstructive Pulmonary Tuberculosis patients in which they have noted that there is considerable decline of Lung function year after year after completion of treatment.[4]

According to Mohammed Al-Hajjaj that lung function improves as duration after treatment increases because of continuous healing process. [54] This was also observed in the present study in a minor group (only13 subjects) who had normal study pattern in Spirometry even though the mean duration after treatment for them was around 43 months compared to subjects who had severe restriction whose mean duration after treatment was around 41 months only.

LAG TIME AND LUNG FUNCTION IMPAIRMENT

In the present study a negative correlation between lag time and values of pulmonary function parameters was observed. This is similar to the study by Eric Walter who states that long duration prior to TB diagnosis is an important predictive factor for persisting respiratory signs following successful treatment. Delay in diagnosis of TB has shown a direct relationship with severity of pulmonary damage. [48]

NUMBER OF EPISODES OF TREATMENT AND LUNG FUNCTION IMPAIRMENT

Negative correlation was observed between decline in Lung function parameters and number of episodes of TB treatment in this study. This is consistent with Eva Hnizdo et al who had quantified the loss of lung function and their relation with number of episodes of Tuberculosis treatment. They say that the increase in number of episodes of treatment corresponded with increase in loss of lung function. [33]

LIMITATIONS

1. This is a retrospective study and all the data obtained for the study like treatment history, personal history, etc. Except the investigations were collected from old records of the subjects.
2. Interpretation of restrictive and mixed pattern of lung function impairment can be made more accurate by measuring Total Lung Capacity, Functional Residual Capacity and Residual Volume by Pulmonary Function Tests other than Spirometry.
3. Periodical follow-up studies at regular intervals with Spirometry can completely assess the impairment of lung function.

CONCLUSION

The present study shows that because of the marked residual changes in the Lung caused by Tuberculosis infection, there occurs a considerable and significant decline in Lung function in post treatment period.

In this study the pattern of impairment of lung function noticed was restrictive pattern, mixed pattern and the extent of impairment increases as lag time, number of episodes of treatment and duration after treatment increases.

As we have limited resources for the management of restrictive and mixed pattern of impairment it is essential that an early and effective intervention is necessary for detection, diagnosis and compliance of treatment in pulmonary tuberculosis affected individuals.

This study again like many other studies stresses that even after successful completion of anti-Tuberculosis treatment, a regular periodical assessment of pulmonary functions with simple and feasible method like Spirometry and addition of Pulmonary Rehabilitation Program along with Anti Tuberculosis treatment is necessary to improve the Quality of Life of the individuals affected by Pulmonary Tuberculosis to a greater extent which helps them to lead a symptomless, comfortable and fruitful life in future.

SUMMARY

- The present study was done to analyze the pattern of Lung function impairment in Pulmonary Tuberculosis sequelae patients.
- 120 subjects both male and female of age group 30-60 years attending Thoracic Medicine outpatient department participated in the study.
- Spirometry was done for the study group using Easy On PC spirometer in the outpatient department itself.
- Both Flow vs Time Graph and Flow Volume Loop were recorded. Percentage of predicted values of FVC, FEV_1, FEV_1/FVC AND $FEF_{25-75\%}$ were taken for analysis.
- Restrictive pattern and mixed pattern of Lung Function Impairment was observed in majority of the subjects. Few subjects (13 out of 120) showed normal study in spirometry.
- This study proves that residual damage do occur in Lungs even after completion of Anti- Tuberculosis treatment and the severity of residual damage depends upon three important factors like lag time, number of episodes of treatment, duration after completion of treatment.
- Hence a regular follow up assessment of Lung function in Pulmonary Tuberculosis patients is essential even after successful completion of Anti- TB treatment to reduce the morbidity and mortality in these individuals.

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ANNEXURES

PROFORMA

Name:

Age:

Sex:

Height:

Weight:

Occupation:

Socioeconomic status:

Present complaints with duration:

Past history:

- H/O pulmonary tuberculosis with duration
- Duration between diagnosis and start of treatment
- Adherence to treatment
- Released from treatment – duration
- H/O HIV
- H/O cardiovascular disease
- H/O any other respiratory illness
- H/O lung surgery
- H/O connective tissue disease
- H/O diabetes mellitus / hypertension

Treatment history:

- Details of Anti-Tuberculosis treatment
- Any side effects for the drugs
- Present treatment

Personal history:

- H/O smoking
- H/O alcoholism

Family history:

- H/O similar illness in family members

Clinical examination:

- Vital signs
- General examination
- Examination of respiratory system
- Examination of cardiovascular system

Investigations:

- Sputum for Acid Fast Bacilli
- Chest X-ray PA view
- Electrocardiogram
- Spirometry

CONSENT FORM

STUDY DETAIL :

"FUNCTIONAL EVALUATION IN PULMONARY TUBERCULOSIS SEQUELAE PATIENTS IN A TERTIARY CARE CENTRE – CHENGALPATTU"

STUDY CENTRE :

THORACIC MEDICINE OP, CHENGALPATTU MEDICAL COLLEGE HOSPITAL, CHENGALPATTU.

PATIENT NAME: AGE: SEX:

IDENTIFICATION NUMBER:

I confirm that have understood the purpose of procedure for the above study.

I have the opportunity to ask question and all my questions and doubts have been answered to my satisfaction.

I understand that my participation in the study is voluntary and that I am free to withdraw anytime without giving any reasons, without my legal rights being affected.

I understand that my investigator, regulatory authorities and the ethics committee will not need my permission to look at my health records both in respect to the current study and any further research that may be conducted in relation to it,

even if I withdraw from the study, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arrives from the study.

I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team.

I hereby give consent to participate in this study.

I hereby give permission to undergo complete clinical examination and diagnostic test.

Signature of investigator Signature/Thumb impression of participant

Date: Participant's address:

Place:

MASTER CHART

MASTER CHART

S NO	NAME	AGE (yrs)	SEX	HEIGHT (cm)	WEIGHT (kg)	BMI	FVC	FEV1	FEV1/FVC	FEF 25-75%	DIAGNOSIS	Lag Time (days)	No. of Episodes of Anti-TB Treatment	Duration After Treatment (months)
1	DURAIBABU	54	M	142	70	34.7	68	64	106	50	MILD RESTRICTION	30	1	25
2	KARTHIKEYAN	30	M	152	45	19.5	49	47	104	46	MODERATE RESTRICTION	180	1	19
3	SULOCHANA	50	F	144	42	20.0	99	89	90	65	NORMAL STUDY	30	1	38
4	KASTHURI	36	F	149	41	18.5	62	76	82	37	MILD RESTRICTION	30	1	38
5	MUNUSAMY	57	M	160	52	20.3	49	46	107	23	MODERATE RESTRICTION	180	1	24
6	MURUGESAN	55	M	157	49	19.9	35	42	90	22	SEVERE RESTRICTION	240	3	24
7	GANESAN	57	M	157	45	18.3	64	72	89	37	MILD RESTRICTION	75	1	24
8	HARIRAMAN	50	M	171	62	21.2	46	49	94	73	MODERATE RESTRICTION	270	2	25
9	VELAYUTHAM	57	M	163	40	15.1	61	68	90	19	MILD RESTRICTION	120	1	37
10	EZHUMAZHAI	50	M	161	44	17.0	61	68	90	50	MILD RESTRICTION	60	1	36
11	THENAPPAN	59	M	154	50	21.1	49	43	114	22	MODERATE RESTRICTION	210	1	24
12	PERIYASAMY	52	M	156	39	16.0	37	22	61	11	MIXED PATTERN	90	2	30
13	MUTHUKRISHNAN	50	M	158	45	18.0	85	85	101	81	NORMAL STUDY	60	1	24
14	OSURAAN	51	M	165	68	25.0	68	60	113	26	MILD RESTRICTION	90	2	18
15	SAKTHIVEL	39	M	164	50	18.6	52	44	118	26	MODERATE RESTRICTION	150	1	40
16	PARAMANANTHAM	58	M	169	66	23.1	69	70	99	69	MILD RESTRICTION	60	1	54
17	CHINAPAYYAN	56	M	156	59	24.2	35	20	59	10	MIXED PATTERN	330	2	60
18	MUMTAJ	56	F	146	36	16.9	95	92	95	68	NORMAL STUDY	30	1	60
19	PATCHAIYAMMAL	46	F	153	38	16.2	39	35	88	20	SEVERE RESTRICTION	180	2	30
20	SARASU	50	F	161	51	19.7	55	55	100	52	MODERATE RESTRICTION	60	1	24
21	GURUNATHAN	55	M	156	44	18.1	80	77	104	62	MILD RESTRICTION	45	1	36
22	SAROJA	39	F	155	65	27.1	71	69	103	50	MILD RESTRICTION	60	1	42
23	MARI	55	M	154	35	14.8	41	48	77	15	SEVERE RESTRICTION	210	2	36
24	DASS	52	M	160	60	23.4	64	72	89	24	MILD RESTRICTION	45	1	44
25	INDHUMATHY	35	F	148	57	26.0	66	68	97	71	MILD RESTRICTION	30	1	24
26	MURUGESAN	53	M	147	52	24.1	53	44	120	22	MODERATE RESTRICTION	150	1	36
27	SRIRANGAN	58	M	157	56	22.7	62	36	58	18	MIXED PATTERN	240	2	60
28	SELVI	30	F	160	50	19.5	46	32	70	15	MIXED PATTERN	360	2	48
29	GOVINDAMMAL	50	F	149	56	25.2	59	49	120	29	MODERATE RESTRICTION	240	1	19

S NO	NAME	AGE (yrs)	SEX	HEIGHT (cm)	WEIGHT (kg)	BMI	FVC	FEV1	FEV1/FVC	FEF 25-75%	DIAGNOSIS	Lag Time (days)	No. of Episodes of Anti-TB Treatment	Duration After Treatment (months)
30	KANNAN	55	M	163	41	15.4	51	49	104	29	MODERATE RESTRICTION	270	1	24
31	CHINNATHAMBI MARI	57	M	169	36	12.6	29	16	56	7	MIXED PATTERN	270	3	60
32	MUNUSAMY VEERABATHRAN	58	M	165	59	21.7	35	43	92	25	SEVERE RESTRICTION	180	2	20
33	AMIRTHAMMAL	50	F	149	46	20.7	45	40	88	25	SEVERE RESTRICTION	210	1	36
34	KESAVAN	57	M	169	56	19.6	25	17	70	10	MIXED PATTERN	240	2	60
35	PARTHASARATHY	42	M	164	49	18.2	42	48	89	29	SEVERE RESTRICTION	240	1	60
36	ARASAMMAL	42	F	157	35	14.2	42	45	84	20	SEVERE RESTRICTION	120	2	60
37	ANNAPPAN	51	M	158	46	18.4	67	73	92	33	MILD RESTRICTION	90	1	24
38	RAJAMMAL	57	F	146	52	24.4	93	94	100	80	NORMAL STUDY	60	1	48
39	MALLIGA	47	F	153	40	17.1	31	22	71	11	MIXED PATTERN	300	2	44
40	VELU	55	M	155	49	20.4	60	69	87	120	MILD RESTRICTION	60	1	46
41	VENGAPPAN	52	M	159	54	21.4	34	48	93	24	SEVERE RESTRICTION	330	3	36
42	BALARAMAN	60	M	159	45	17.8	72	74	97	73	MILD RESTRICTION	30	1	48
43	SALAMMAL	52	F	148	70	32.0	42	46	97	31	SEVERE RESTRICTION	270	1	54
44	VEERARAGHAVAN	60	M	169	49	17.2	40	22	54	12	MIXED PATTERN	330	1	54
45	DHANASEKARAN	60	M	157	54	21.9	46	52	88	21	MODERATE RESTRICTION	300	1	42
46	SHANMUGAM	60	M	148	54	24.9	45	58	78	32	MODERATE RESTRICTION	360	1	30
47	RANGASAMY	57	M	149	46	20.7	48	49	98	32	MODERATE RESTRICTION	210	2	27
48	KARUMPAYEE	44	F	142	42	20.8	32	20	65	8	MIXED PATTERN	270	3	48
49	CARMELRAJ	52	M	158	43	17.2	43	51	80	18	SEVERE RESTRICTION	150	2	60
50	VELU VENKATESAN	38	M	149	40	18.0	35	16	46	8	MIXED PATTERN	360	2	24
51	MANI	50	M	171	60	20.5	46	62	74	24	MODERATE RESTRICTION	150	1	24
52	RAJA	45	M	168	54	19.1	51	60	85	47	MODERATE RESTRICTION	60	1	48
53	PONNUSAMY	40	M	168	68	24.1	52	61	85	46	MODERATE RESTRICTION	30	2	60
54	RADHA	40	F	153	60	25.6	39	48	97	32	SEVERE RESTRICTION	240	2	24
55	PUVIARASI	48	F	153	40	17.1	73	76	96	87	MILD RESTRICTION	105	2	36
56	VADIVEL	60	M	142	40	19.8	52	50	104	40	MODERATE RESTRICTION	210	1	43
57	NAGAMMAL	59	F	147	35	16.2	47	31	65	13	MIXED PATTERN	270	2	60
58	KANNIAPPAN	35	M	170	66	22.8	60	72	83	31	MILD RESTRICTION	60	1	48
59	MOHAN	35	M	155	55	22.9	69	64	108	50	MILD RESTRICTION	30	1	42
60	KARTHICK	32	M	176	52	16.8	62	68	91	71	MILD RESTRICTION	75	1	60
61	MANI	32	M	168	50	17.7	34	42	76	11	SEVERE RESTRICTION	90	1	18

S NO	NAME	AGE (yrs)	SEX	HEIGHT (cm)	WEIGHT (kg)	BMI	FVC	FEV1	FEV1/FVC	FEF 25-75%	DIAGNOSIS	Lag Time (days)	No. of Episodes of Anti-TB Treatment	Duration After Treatment (months)
62	EZHUMAZHAI	51	M	160	68	26.6	80	84	105	51	NORMAL STUDY	30	1	48
63	SATHYASEELAN	59	M	162	54	20.6	48	30	63	14	MIXED PATTERN	300	1	43
64	DHANAPAL	53	M	162	69	26.3	53	59	90	37	MODERATE RESTRICTION	300	2	36
65	RAJU	35	M	159	53	21.3	43	28	66	13	MIXED PATTERN	240	1	56
66	DEVI	33	F	153	56	23.9	76	80	95	102	MILD RESTRICTION	30	1	36
67	KATHAVARAYAN THANGAVEL	57	M	160	56	21.9	66	72	92	76	MILD RESTRICTION	90	1	19
68	KATHAVARAYAN VELAN	60	M	164	55	20.4	62	70	89	24	MILD RESTRICTION	30	2	42
69	GAJAPATHY	51	M	170	40	13.8	47	32	67	18	MIXED PATTERN	330	1	60
70	DHANAPAL MANI	46	M	157	45	18.3	57	61	93	34	MODERATE RESTRICTION	150	2	52
71	ANTHONYAMMAL	47	F	158	40	16.0	46	58	79	32	MODERATE RESTRICTION	240	1	60
72	PUSHPA	57	F	147	54	25.0	35	45	89	18	SEVERE RESTRICTION	60	2	56
73	EZHILARASI	44	F	150	60	26.7	54	58	93	30	MODERATE RESTRICTION	60	2	60
74	GOVINDAMMAL	39	F	149	38	17.1	63	67	94	46	MILD RESTRICTION	120	1	20
75	MANOHARAN	48	M	156	54	22.2	68	70	97	82	MILD RESTRICTION	60	1	25
76	NAGALINGAM	45	M	157	55	22.3	58	37	64	15	MIXED PATTERN	330	3	60
77	MANI	48	M	155	43	18.0	88	92	105	97	NORMAL STUDY	75	1	51
78	SINGARAVELU	58	M	154	52	22.0	67	73	92	68	MILD RESTRICTION	90	1	47
79	KASINATHAN	57	M	152	43	18.6	58	53	109	35	MODERATE RESTRICTION	90	2	27
80	FATHIMA	30	F	152	68	29.4	61	68	90	51	MILD RESTRICTION	105	2	24
81	SIVAKUMAR	35	M	172	49	16.6	36	44	82	18	SEVERE RESTRICTION	210	2	60
82	REVATHY	31	F	156	60	24.7	49	30	61	12	MIXED PATTERN	60	2	49
83	RAMALINGAM	41	M	163	45	16.9	56	65	86	26	MODERATE RESTRICTION	330	1	24
84	KUMAR	39	M	160	54	21.1	73	70	104	63	MILD RESTRICTION	90	1	24
85	RAMESHKUMAR	32	M	170	70	24.2	66	66	100	71	MILD RESTRICTION	60	1	18
86	RAGHAVAN	58	M	152	55	23.8	55	58	95	20	MODERATE RESTRICTION	240	1	48
87	VASANTHI	43	F	152	52	22.5	67	72	93	86	MILD RESTRICTION	60	1	36
88	PANCHATCHARAM	37	M	163	70	26.3	56	66	85	22	MODERATE RESTRICTION	90	1	36
89	ARUNA	44	F	145	40	19.0	70	66	106	57	MILD RESTRICTION	105	2	39
90	SARITHA	57	F	139	65	33.6	49	55	89	31	MODERATE RESTRICTION	210	2	52
91	ANAR	45	F	154	60	25.3	63	67	94	58	MILD RESTRICTION	75	1	36
92	SHOBHIKA	30	F	153	47	20.1	86	82	96	69	NORMAL STUDY	30	1	57

S NO	NAME	AGE (yrs)	SEX	HEIGHT (cm)	WEIGHT (kg)	BMI	FVC	FEV1	FEV1/FVC	FEF 25-75%	DIAGNOSIS	Lag Time (days)	No. of Episodes of Anti-TB Treatment	Duration After Treatment (months)
93	SWETHA	38	F	143	52	25.4	74	68	109	46	MILD RESTRICTION	30	1	48
94	MALARKODI	40	F	150	45	20.0	94	96	102	88	NORMAL STUDY	45	1	42
95	ANITHA	49	F	151	60	26.3	96	94	98	77	NORMAL STUDY	60	1	48
96	PALANI	50	M	150	55	24.4	60	65	92	59	MILD RESTRICTION	30	1	21
97	MURUGAN	50	M	157	54	21.9	81	87	109	98	NORMAL STUDY	60	1	24
98	KABILAN	50	M	160	54	21.1	52	53	98	56	MODERATE RESTRICTION	45	1	24
99	KANNAN	57	M	154	50	21.1	83	92	111	111	NORMAL STUDY	60	1	36
100	VEERASAMY	49	M	140	55	28.1	61	66	92	49	MILD RESTRICTION	60	1	24
101	VASANTH	51	M	157	50	20.3	76	83	92	96	MILD RESTRICTION	30	1	36
102	NASEEM	35	M	143	55	26.9	60	72	83	35	MILD RESTRICTION	30	1	24
103	RAJAGOPAL	60	M	172	52	17.6	63	68	93	31	MILD RESTRICTION	105	1	26
104	PAVULUS	57	M	156	44	18.1	72	68	106	36	MILD RESTRICTION	30	1	24
105	JEYANTHI	37	F	142	70	34.7	54	50	108	38	MODERATE RESTRICTION	90	2	48
106	KUPPAN	46	M	159	40	15.8	48	33	69	18	MIXED PATTERN	270	2	60
107	MUNIAMMAL	45	F	145	45	21.4	51	66	77	29	MODERATE RESTRICTION	75	2	25
108	CHANDRASEKAR	58	M	158	69	27.6	61	68	90	64	MILD RESTRICTION	30	2	38
109	KUMAR	32	M	175	63	20.6	87	81	93	65	NORMAL STUDY	60	1	25
110	RADHA	32	F	168	67	23.7	55	51	108	33	MODERATE RESTRICTION	180	2	36
111	SUDHA	35	F	151	70	30.7	90	85	94	64	NORMAL STUDY	45	1	60
112	MUNEESWARI	30	F	154	70	29.5	61	66	92	66	MILD RESTRICTION	30	1	30
113	SHANKARI	32	F	168	68	24.1	64	64	100	38	MILD RESTRICTION	45	1	48
114	RAVI	48	M	160	70	27.3	36	24	67	11	MIXED PATTERN	180	2	46
115	GOTHANDAM	47	M	168	58	20.5	55	56	98	61	MODERATE RESTRICTION	30	1	36
116	SHANKARI	50	F	160	65	25.4	29	30	63	14	MIXED PATTERN	150	2	48
117	VELLAPPAN	57	M	158	60	24.1	51	32	64	15	MIXED PATTERN	210	2	50
118	VEERABATHIRAN	55	M	169	63	22.1	53	66	80	29	MODERATE RESTRICTION	270	1	60
119	MANNU	55	M	170	70	24.2	26	51	51	23	MODERATE RESTRICTION	60	1	55
120	RADHAKRISHNAN	55	M	168	51	18.1	47	31	67	19	MIXED PATTERN	120	1	60